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AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s bone marrow
L1 369490 BONE MARROW

=> s l1 and (HIF or endothelial PAS domain protein 1 or EPAS1 or MCP 1 or GM
CSF or PR39 or FGF or NOS)
L2 12787 L1 AND (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR
EPAS1 OR MCP
1 OR GM CSF OR PR39 OR FGF OR NOS)

=> s adenovir? (3a) vector
L3 26915 ADENOVIR? (3A) VECTOR

=> s l2 and l3
L4 54 L2 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 50 DUP REM L4 (4 DUPLICATES REMOVED)

=> d bib abs 1-
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L5 ANSWER 1 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
reserved on STN
AN 2006586638 EMBASE <<LOGINID::20070126>>
TI Adenoviral-encoded antigens are presented efficiently by a subset of
dendritic cells expressing high levels of .alpha.(v).beta.(3) integrins.
AU Harui A.; Roth M.D.; Vira D.; Sanghi M.; Mizuguchi H.; Basak S.K.
CS S.K. Basak, Division of Pulmonary and Critical Care, Department of
Medicine, UCLA School of Medicine, Los Angeles, CA 90095-1690, United
States. sbasak@mednet.ucla.edu
SO Journal of Leukocyte Biology, (2006) Vol. 79, No. 6, pp. 1271-1278.
Refs: 33
ISSN: 0741-5400 CODEN: JLBIE7
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 14 Dec 2006
Last Updated on STN: 14 Dec 2006
AB Dendritic cells (DC) play a central role in antigen presentation and are
often targeted by adenoviral (Ad)-based gene therapy. However, DC lack
the coxsackie-Ad receptor, and little is known about the process by which
they acquire and present Ad-encoded antigens. We examined the expression
of .alpha.(v).beta.(3) integrins (CD51/CD61) on mouse ***bone***
marrow-derived DC (BM-DC) and their susceptibility to transduction
by Ad vectors. Less than 10% of BM-DC precursors expressed CD51, but
expression increased over time in culture with granulocyte
macrophage-colony stimulating factor (***GM*** - ***CSF***
)/interleukin (IL)-4. After 7 days, 28 +/- 1.7% of CD11c (+) DC
expressed high levels of CD51 (CD51(hi)), and the remaining DC expressed
low levels of CD51 (CD51(lo)). CD51(hi) DC express higher major
histocompatibility complex type 1 (MHC I); however, both of the DC subsets
expressed similar levels of MHC II and costimulatory molecules. When
exposed to a first-generation Ad vector, transgene expression was
restricted to the CD51(hi) DC subset and blocked by soluble peptides
expressing an arginine, glycine, aspartic acid (RGD) sequence, confirming
the role of integrins in viral entry. Consistent with this, a modified Ad
expressing an RGD-binding sequence in its fiber knob (Ad-RGD) transduced
the CD51(hi) DC subset with significantly higher efficiency. When BM-DC
were transduced with an Ad-expressing ovalbumin (Ad-OVA), the CD51(hi)
subset proved superior in activating OT-I (T cell receptor-OVA) T cells.
Similar to in vitro effects, systemic administration of ***GM*** -
CSF /IL-4 increased the expression of CD51 on splenic DC and
rendered these cells susceptible to Ad transduction. These results
suggest that a limited subset of DC expressing high levels of
.alpha.(v).beta.(3) integrins is preferentially transduced by Ad vectors
and activates CD8 (+) T cell responses against Ad-encoded antigens.
COPYRG: Society for Leukocyte Biology.

L5 ANSWER 2 OF 50 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2006:744682 CAPLUS <<LOGINID::20070126>>
TI Evaluation of permissiveness and cytotoxic effects in equine chondrocytes,
synovial cells, and stem cells in response to infection with adenovirus 5
vectors for gene delivery
AU Ishihara, Akikazu; Zachos, Terri A.; Bartlett, Jeffrey S.; Bertone, Alicia
L.
CS Comparative Orthopedic Molecular Medicine Laboratory, Department of
Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio
State University, Columbus, OH, 43210, USA
SO American Journal of Veterinary Research (2006), 67(7), 1145-1155
CODEN: AJVRAH; ISSN: 0002-9645
PB American Veterinary Medical Association
DT Journal
LA English
AB Objective-To evaluate host cell permissiveness and cytotoxic effects of
recombinant and modified adenoviral vectors in equine chondrocytes,
synovial cells, and ***bone*** ***marrow***-derived mesenchymal
stem cells (BMD-MSCs). Sample Population-Articular cartilage, synovium,
and ***bone*** ***marrow*** from 15 adult horses.
Procedures-Equine chondrocytes, synovial cells, and BMD-MSCs and human

carcinoma (HeLa) cells were cultured and infected with an E-1-deficient ***adenovirus*** encoding the .beta.-galactosidase gene or the green fluorescent protein gene (Ad-GFP) and with a modified E-1-deficient vector with the arg-gly-asp capsid peptide insertion and contg. the GFP gene (Ad-RGD-GFP). Percentages of transduced cells, total and transduced cell counts, and cell viability were assessed 2 and 7 days after infection. Results-Permissiveness to ***adenoviral*** infection was significantly different among cell types and was ranked in decreasing order as follows: HeLa cells > BMD-MSCs > chondrocytes > synovial cells. Morphol. signs of cytotoxicity were evident in HeLa cells but not in equine cells. ***Nos*** of transduced cells decreased by day 7 in all cell types except equine BMD-MSCs. Transduction efficiency was not significantly different between the Ad-GFP and Ad-RGD-GFP vectors. Conclusion and Clin. Relevance-Sufficient gene transfer may be achieved by use of an ***adenovirus*** ***vector*** in equine cells. High vector doses can be used in equine cells because of relative resistance to cytotoxic effects in those cells. Greater permissiveness and sustained expression of transgenes in BMD-MSCs make them a preferential cell target for gene therapy in horses.

RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L5 ANSWER 3 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2006629839 EMBASE <<LOGINID::20070126>>
TI ***GM*** - ***CSF*** gene-modified cancer cell immunotherapies: Of mice and men.
AU Hege K.M.; Jooss K.; Pardoll D.
CS Dr. K.M. Hege, Cell Genesys, Inc., 500 Forbes Blvd., South San Francisco, CA 94080, United States. kristen.hege@cellgenesys.com
SO International Reviews of Immunology, (1 Dec 2006) Vol. 25, No. 5-6, pp. 321-352.
Refs: 99
ISSN: 0883-0185 E-ISSN: 1563-5244 CODEN: IRIMEH
PUI G1867322KM177569
CY United Kingdom
DT Journal; General Review
FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA English
SL English
ED Entered STN: 24 Jan 2007
Last Updated on STN: 24 Jan 2007
AB GVAX cancer immunotherapies are composed of whole tumor cells genetically modified to secrete the immune stimulatory cytokine, granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***), and then irradiated to prevent further cell division. Both autologous (patient specific) and allogeneic (non-patient specific) GVAX platforms have been evaluated either as single agents or in combination with other immunomodulatory strategies. Many early-phase clinical trials have now been completed. Results have consistently demonstrated a favorable safety profile manifested primarily by injection site reactions and flu-like symptoms. Consistent evidence of immune activation and clinical activity, including radiologic tumor regressions, has been seen across multiple cancer indications in both early- and late-stage disease. Phase 3 trials evaluating an allogeneic GVAX immunotherapy product in prostate cancer are under way. Copyright .COPYRGT. Informa Healthcare.

L5 ANSWER 4 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:44414 CAPLUS <<LOGINID::20070126>>
DN 144:231195
TI Recombinant Adenovirus Vaccines Can Successfully Elicit CD8+ T Cell Immunity under Conditions of Extreme Leukopenia
AU Grinshtein, Natalie; Yang, Teng-Chih; Parsons, Robin; Millar, James; Denisova, Galina; Dissanayake, Dilan; Leitch, Jaina; Wan, Yonghong; Bramson, Jonathan
CS Department of Pathology and Molecular Medicine, Center for Gene Therapeutics, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SO Molecular Therapy (2006), 13(2), 270-279
CODEN: MTOHCK; ISSN: 1525-0016
PB Elsevier
DT Journal
LA English

AB The authors have examd. the efficacy of vaccination with recombinant adenovirus under conditions of extreme leukopenia in lethally irradiated mice reconstituted with autologous ***bone*** ***marrow***. The expansion of antigen-specific CD8+ T cells following immunization of lethally irradiated hosts paralleled the recovery of total CD8+ T cells. Surprisingly, the ***nos*** of antigen-specific CD8+ T cells in lethally irradiated mice beyond 6 wk postimmunization were comparable to the ***nos*** found in nonirradiated controls. CD8+ T cells elicited in the lethally irradiated hosts were functionally indistinguishable from those elicited in normal hosts. Antigen expression and presentation persisted for a longer period of time in the draining lymph nodes of irradiated mice compared to those of nonirradiated animals, suggesting that antigen presentation mechanisms were intact during the reconstitution period. Expts. employing allogeneic ***bone*** ***marrow*** demonstrated that radioresistant host antigen-presenting cells were

responsible for antigen presentation during the process of immune reconstitution. These results demonstrate clear compatibility of adenovirus vaccines and cytotoxic therapy. Furthermore, these observations provide novel insights into the mechanisms of CD8+ T cell activation following adenovirus immunization.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L5 ANSWER 5 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:158814 CAPLUS <<LOGINID::20070126>>
DN 142:246021
TI Switch/biosensor vector system containing a tissue-specific promoter and a gene encoding a stem cell-attracting chemokine as stem cell beacon, and therapeutic uses
IN Phillips, Ian M.; Tang, Yao Liang
PA University of South Florida, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005017165	A1	20050224	WO 2004-US26196	20040811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2535683	A1	20050224	CA 2004-2535683	20040811
EP 1654366	A1	20060510	EP 2004-780954	20040811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRAI US 2003-494184P	P	20030811		
US 2003-494185P	P	20030811		
US 2003-513067P	P	20031021		
US 2003-513657P	P	20031023		
WO 2004-US26196	W	20040811		
AB The invention relates to methods and compns. for selectively directing stem cells to a target tissue within a subject using a system that employs one or more vectors that contain a gene switch/biosensor, a tissue-specific promoter, a gene encoding a stem cell-attracting chemokine (e.g., stromal-derived factor (SDF)-1.alpha., stem cell factor (SCF)) and a gene amplification system. The gene switch/biosensor allows expression of the chemokine-encoding gene to be regulated by a stimulus (e.g., a physiol. stimulus such as one assocd. with cellular degeneration, cell injury, such as hypoxia or elevated glucose levels). A stem cell-attracting chemokine is expressed in damaged tissue using a stimulus-responsive vector system. Expression of the chemokine increases the trafficking of stem cells to the damaged tissue. Once in the target tissue, the stem cells can differentiate (with or without the help of other agents such as morphogenesis) into new cells to replace the damaged cells and restore organ function.				

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:158813 CAPLUS <<LOGINID::20070126>>
DN 142:233371
TI Viral vector system that detects and responds to pathophysiological stimulus, grafted transgenic vigilant stem cells containing same, and therapeutic uses
IN Phillips, Ian M.; Tang, Yao Liang
PA University of South Florida, USA
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005017164	A1	20050224	WO 2004-US26195	20040811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2535680	A1	20050224	CA 2004-2535680	20040811
EP 1654365	A1	20060510	EP 2004-780953	20040811

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRAI US 2003-494184P P 20030811
US 2003-494185P P 20030811
US 2003-513067P P 20031021
US 2003-513657P P 20031023
WO 2004-US26195 W 20040811

AB ***Bone*** ***marrow*** -derived mesenchymal stem cells were transduced with a stimulus-responsive rAAV vector system that detects and responds to hypoxia in cardiac tissue. The first rAAV vector in the system is the "sensor" vector, and contains a cardiac-specific promoter linked to a sequence encoding an oxygen-sensitive chimeric transactivator contig, a GAL4 DNA binding domain (DBD), an oxygen-dependent degrdn. domain from ***HIF*** -1.alpha., and a NF-kappa.B p65 activation domain (AD). The second rAAV vector is the "effector" vector, and contains a cardioprotective gene, such as heme oxygenase-1 gene, linked to a GAL4 UAS. The first rAAV vector expresses the chimeric transactivator specifically in the heart, and in response to hypoxia, the transactivator binds to the GAL4 upstream activating sequence (UAS) in the second rAAV vector. Binding of the transactivator to the UAS results in the expression of the cardioprotective gene. The rAAV vectors can be used to treat cells in a no. of other disease states, including diabetes, cancer, stroke, and atherosclerosis. These approaches to stem cell-based gene therapy provide a novel strategy not only for treatment but for prevention of cell destruction.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L5 ANSWER 7 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2005:536008 BIOSIS <<LOGINID::20070126>>

DN PREV200510321511

TI Endothelial nitric oxide synthase (eNOS) gene-transfected vascular prosthesis with ***bone*** ***marrow*** cell transplantation.

AU Horimoto, Sachiko [Reprint Author]; Mieno, Shigetoshi; Horimoto, Hitoshi; Kishida, Kenji; Watanabe, Fusao; Furuya, Eisuke; Katsumata, Takahiro
CS Osaka Med Coll, Dept Thorac and Cardiovasc Surg, Osaka 5698686, Japan
SO FASEB Journal, (MAR 7 2005) Vol. 19, No. 5, Suppl. S, Part 2, pp. A1677.

Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences, San Diego, CA, USA, March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci. CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 Dec 2005

Last Updated on STN: 1 Dec 2005

AB Introduction; Therapeutic angiogenesis by ***bone*** ***marrow*** cell (BMC) transplantation has been clinically available for the treatment of ischemic cardiovascular disease. Endothelial nitric oxide synthase (eNOS) is an attractive target of cardiovascular gene therapy to elicit angiogenic, cytoprotective and vasculoprotective effects. Herein, we attempted to develop vascular prosthesis (VP) generating enzymatic activity of eNOS by using gene-engineering. Method; The replication-deficient adenovirus was constructed harboring rat eNOS cDNA and beta galactosidase (beta gal) cDNA under the control of the cytomegalovirus promoter. The BMCs were isolated from six-week male SD rats and transfected with each adenovirus (eNOS/BMC, beta gal/BMC, respectively). The beta gal/BMC was impregnated into VP, then the expressions of beta gal was evaluated by X-gal stain. The ***NOS*** activity of eNOS/BMC was assayed by monitoring the conversion of H-3-arginine to 3 H-citrulline. Result; The luminal surface of the VP was covered with BMC expressing beta gal. The amount of the H-3-citrulline was increased and eNOS/BMC was determined to generate enzymatic activity of eNOS. Conclusion; These data suggest that eNOS/BMC preserves valid biochemical property of eNOS, implicating that eNOS gene-transfected VP can exert enzymatic activity of eNOS. Results of the present study may lead to development of a novel clinical relevant VP.

L5 ANSWER 8 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:681685 CAPLUS <<LOGINID::20070126>>

DN 141:185593

TI Methods for modulating stem cells recruitment, proliferation and differentiation with VEGF-B and PDGF and therapeutic uses thereof

IN Alitalo, Kari; Enksson, Ulf; Carmeliet, Peter; Li, Xuri; Collen, Desire; Yla-Herttuala, Seppo; Salven, Petri; Rajantie, Iiro

PA Ludwig Institute for Cancer Research, USA; Licentia, Ltd.; Flanders Interuniversity Institute for Biotechnology

SO PCT Int. Appl., 151 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004070018	A2	20040819	WO 2004-US3316	20040204
WO 2004070018	A3	20050203		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004209668 A1 20040819 AU 2004-209668 20040204
US 2004248796 A1 20041209 US 2004-772927 20040204
EP 1594527 A2 20051116 EP 2004-708229 20040204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006517586 T 20060727 JP 2006-503352 20040204

PRAI US 2003-445021P P 20030204

US 2003-471412P P 20030516

WO 2004-US3316 A 20040204

AB The present invention provides materials and methods for VEGF-B AND PDGF

therapy, esp. therapy directed at stem cell recruitment, proliferation, and/or differentiation.

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AN 2004065184 EMBASE <<LOGINID::20070126>>

TI Role of Immature Myeloid Gr-1(+) Cells in the Development of Antitumor Immunity.

AU Li Q.; Pan P.-Y.; Gu P.; Xu D.; Chen S.-H.

CS S.-H. Chen, C. C. I. Inst. Gene Ther./Mol. Med., Box 1496, Mount Sinai

School of Medicine, One Gustave L. Levy Place, New York, NY 10029, United States. Shu-Hsia.Chen@mssm.edu

SO Cancer Research, (1 Feb 2004) Vol. 64, No. 3, pp. 1130-1139.

Refs: 66

ISSN: 0008-5472 CODEN: CNREAA

CY United States

DT Journal; Article

FS 016 Cancer

037 Drug Literature Index

LA English

SL English

ED Entered STN: 11 Mar 2004

Last Updated on STN: 11 Mar 2004

AB One of the mechanisms by which tumor cells evade the immune system is the lack of proper antigen-presenting cells. Improvement in host immunity against tumor cells can be achieved by promoting the differentiation of dendritic cells (DCs) from immature myeloid cells (Gr-1(+)Ly-6C(+)F4/80(+) that accumulate in the ***bone*** ***marrow*** and lymphoid organs of mice with large tumor burdens. The enriched immature myeloid cells inhibit T-cell proliferation and tumor-specific T-cell response, which can be reversed by the differentiation of immature myeloid cells or depletion of F4/80(+) cells. Sorted Gr-1(+)F4/80(+) immature myeloid cells differentiated into CD11c(+) cells that express CD80 and I-A/I-E (MHC class II) in the presence of recombinant murine granulocyte macrophage colony-stimulating factor (***GM*** - ***CSF***). Furthermore, intratumoral gene delivery of ***GM*** - ***CSF*** not only promoted the differentiation of carboxyfluorescein succinimidyl ester-labeled immature myeloid cells into CD11c(+) cells with the characteristics of mature DCs (CD80(+) , I-A/I-E(+)) but also enhanced innate natural killer and adaptive cytolytic T-cell activities in mice treated with interleukin (IL)-12 and anti-4-1BB combination therapy. More importantly, intratumoral delivery of ***GM*** - ***CSF*** and IL-12 genes in combination with 4-1BB costimulation greatly improved the long-term survival rate of mice bearing large tumors and eradicated the untreated existing hepatic tumor. The results suggest that inducing the maturation of immature myeloid cells, thus preventing their inhibitory activity and enhancing their antigen-presenting capability, by ***GM*** - ***CSF*** gene therapy is a critically important step in the development of effective antitumor responses in hosts with advanced tumors.

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AN 2004200648 EMBASE <<LOGINID::20070126>>

TI Route of administration influences the antitumor effects of ***bone*** ***marrow*** -derived dendritic cells engineered to produce interleukin-12 in a metastatic mouse prostate cancer model.

AU Saika T.; Satoh T.; Kusaka N.; Ebara S.; Mouraviev V.B.; Timme T.L.; Thompson T.C.

CS Dr. T.C. Thompson, 6560 Fannin, Houston, TX 77030, United States.

timothy.t@www.urol.bcm.tmc.edu

SO Cancer Gene Therapy, (2004) Vol. 11, No. 5, pp. 317-324.

Refs: 35

ISSN: 0929-1903 CODEN: CGTGEH

CY United States

DT Journal; Article

FS 016 Cancer

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LA English

SL English

ED Entered STN: 28 May 2004

Last Updated on STN: 28 May 2004

AB Gene-modified dendritic cells (DC) provide unique therapeutic strategies for prostate cancer; however, the comparative evaluation of specific delivery options using appropriate preclinical models has not been

described. In this study, ***bone*** ***marrow*** -derived DC were genetically engineered to express high levels of interleukin-12 (IL-12) with or without the costimulatory molecule B7-1, by ex vivo infection with recombinant adenoviral vectors. We used an orthotopic metastatic mouse prostate cancer preclinical model (178-2 BMA) to compare two therapeutic protocols for DC delivery, in situ and subcutaneous. DC were generated from ***bone*** ***marrow*** of syngeneic 129/Sv mice by culturing in the presence of ***GM*** - ***CSF*** and IL-4. In vitro DC/IL-12 or DC/IL-12/B7 produced high levels of biologically active IL-12. In situ delivery of DC/IL-12 or DC/IL-12/B7 induced a significant suppression of primary tumor growth compared to DC/beta.gal controls (P=.0328 and P=.0019, respectively), as well as reduced numbers of spontaneous lung metastatic nodules (P=.1404 and P=.0335, respectively). In survival experiments, in situ DC/IL-12 injection demonstrated a small but statistically significant advantage (P=.0041). Subcutaneous, tumor lysate pulsed DC/IL-12 significantly decreased tumor size (P=.0152) and increased survival (P=.0433) compared to HBSS controls but the decrease in the number of spontaneous lung metastases did not achieve statistical significance. Both in situ and subcutaneous treatments enhanced cytolytic activities of natural killer (NK) cells and cytotoxic T lymphocytes (CTL). In this preclinical model, gene-modified DC-based intratumoral immunotherapy was shown to be an effective therapeutic strategy for locally advanced prostate cancer based on tumor growth suppression, inhibition of metastasis and survival improvement.

L5 ANSWER 11 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:971808 CAPLUS <<LOGINID::20070126>>

DN 140:13049

TI Intramyocardial injection of autologous ***bone*** ***marrow***

IN Epstein, Stephen; Fuchs, Shmuel; Komowski, Ran; Leon, Martine B.; Carpenter, Kenneth W.

PA Myocardial Therapeutics, Inc., USA

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003101201	A1	20031211	WO 2003-US15529	20030516
W: AU, CA, JP				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2487410	A1	20031211	CA 2003-2487410	20030516
AU 2003232152	A1	20031219	AU 2003-232152	20030516
EP 1513404	A1	20050316	EP 2003-756182	20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP 2005527228	T	20050915	JP 2004-508572	20030516
PRAI US 2002-160514	A	20020530		
WO 2003-US15529	W	20030516		

AB Methods are provided for enhancing transfection efficiency of ***bone*** ***marrow*** cells by transfecting early attaching cells derived from ***bone*** ***marrow*** in culture. Methods are also provided for utilizing such early attaching cells derived from autologous ***bone*** ***marrow*** to deliver angiogenesis-promoting transgenes to a patient. The transfected early attaching cells are introduced into an ischemic tissue, such as the heart, to enhance formation of collateral blood vessels. Methods are also provided for treating ischemic muscle by co-administration of autologous ***bone*** ***marrow*** cells and RGTa, for example RGTa11.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2003070017 EMBASE <<LOGINID::20070126>>

TI Rapamycin specifically interferes with ***GM*** - ***CSF*** signaling in human dendritic cells, leading to apoptosis via increased p27(KIP1) expression.

AU Woltman A.M.; Van der Kooij S.W.; Coffey P.J.; Offringa R.; Daha M.R.; Van Kooten C.

CS A.M. Woltman, Leiden University Medical Center, Department of Nephrology, Albinusdreef 2, 2333 ZA Leiden, Netherlands. a.m.woltman@lumc.nl

SO Blood, (15 Feb 2003) Vol. 101, No. 4, pp. 1439-1445.

Refs: 50

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology

026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 27 Feb 2003

Last Updated on STN: 27 Feb 2003

AB The longevity of dendritic cells (DCs) is a critical regulatory factor influencing the outcome of immune responses. Recently, we demonstrated that the immunosuppressive drug rapamycin (Rapa) specifically induces apoptosis in DCs but not in other myeloid cell types. The present study unraveled the mechanism used by Rapa to induce apoptosis in human

monocyte-derived DCs. Our data demonstrate that granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***) preserves DC survival specifically via the phosphatidylinositol-3 lipid kinase/mammalian target of rapamycin (PI3K/mTOR) signaling pathway, which is abrogated by Rapa at the level of mTOR. Disruption of this ***GM*** - ***CSF*** signaling pathway induced loss of mitochondrial membrane potential, phosphatidyl-serine exposure, and nuclear changes. Apoptosis of these nonproliferating DCs was preceded by an up-regulation of the cell cycle inhibitor p27(KIP1). Overexpression of p27(KIP1) in DCs using adenoviral gene transduction revealed that apoptosis is directly regulated by p27(KIP1). Furthermore, both overexpression of p27(KIP1) and disruption of the ***GM*** - ***CSF*** /PI3K/mTOR signaling pathway decreased the expression of the antiapoptotic protein mcl-1. This mTOR/p27(KIP1)/mcl-1 survival seems unique for DCs and may provide novel opportunities to influence immune responses by specific interference with the life span of these cells. .COPYRG. 2003 by The American Society of Hematology.

L5 ANSWER 13 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2004:150380 BIOSIS <<LOGINID::20070126>>

DN PREV200400146928

TI In vitro and in vivo molecular profiling of multiple myeloma (MM) cell interactions with ***bone*** ***marrow*** (MM) microenvironment: Insight into the role of novel anti-MM agents in counteracting BM-mediated drug-resistance in MM.

AU Mitsiades, Constantine S. [Reprint Author]; Mitsiades, Nicholas [Reprint Author]; McMullan, Ciaran J. [Reprint Author]; Poulaki, Vassiliki [Reprint Author]; Shringarpure, Reshma [Reprint Author]; Hideshima, Teru [Reprint Author]; Chauhan, Dharminder [Reprint Author]; Munshi, Nikhil C. [Reprint Author]; Joseph, Marie; Libermann, Towia A.; Anderson, Kenneth C. [Reprint Author]

CS Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 441a. print.

Meeting Info.: 45th Annual Meeting of the American Society of Hematology, San Diego, CA, USA, December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Mar 2004

Last Updated on STN: 17 Mar 2004

AB The response of multiple myeloma (MM) patients to conventional therapies (e.g. Dex, cytotoxic chemotherapy) is significantly attenuated by anti-apoptotic molecular sequelae induced in MM cells by their local ***bone*** ***marrow*** (BM) microenvironment, via BM-derived cytokines, as well as MM cell adhesion to extracellular matrix (ECM) proteins and BM stromal cells (BMSCs). To characterize the molecular sequelae of these microenvironmental interactions and define therapeutic strategies to overcome them, we developed ex vivo and in vivo models of MM cell interactions with their BM milieu and analyzed the gene expression (with U133A Affymetrix microarrays) and proteomic profiles (with multiplex immunoblotting arrays) of MM cells and/or the stromal component. These data were processed bioinformatically, by hierarchical and functional clustering, relevance networks and principal component analyses, and were validated with functional mechanistic assays. The ex vivo interactions were studied in co-culture models of human MM cells and human BMSCs; in vivo interactions were characterized in a SCID/NOD model of diffuse bone lesions of by i.v. injected human MM cells. In both models, we used human MM cell lines (e.g. MM-1S, MM-1R, OPM-1) transduced with retroviral vectors expressing green fluorescent protein (GFP), which allows for rapid flow cytometric sorting of GFP+ MM cells from non-GFP-expressing normal cells, and for differential molecular profiling in the MM vs. stromal component of the BM milieu. The co-culture of MM cells and BMSCs in our model triggered in BMSCs the production of cytokines (e.g. IL-6, VEGF, IGFs or LIF); upregulation of adhesion molecules (e.g. integrin beta5) and 26S proteasome subunits. MM cells co-cultured with BMSCs present with a molecular signature consistent with a composite effect of their in vitro stimulation of MM cells by cytokines (e.g. IGFs and IL-6) and adhesion to stroma or ECM, including activation of PI-3K/Akt and Raf/MAPK signaling pathways; increased transcriptional activity of NF-kappaB and ***HIF*** -1a; upregulation of proteasome subunits and proteasome activity; phosphorylation and functional neutralization of pro-apoptotic Forkhead transcription factors; as well as upregulation of inhibitors of apoptosis (e.g. FLIP, cIAP-2 survivin, Mcl-1), heat shock proteins (e.g. hsp90, hsp70), oncogenic kinases, D-type cyclins, or members of the Wnt pathway (e.g. Wnt-5a). In addition, in vivo molecular profiles of MM cells homing in the BM of SCID/NOD mice were consistent with the profiles of in vitro cytokine- or co-culture-stimulation of MM cells. However, molecular profiles of MM cells treated with novel anti-MM drugs (e.g. hsp90, IGF-1R or proteasome inhibitors), either the in vitro or the in vivo models of interaction with the BM milieu, were consistent with the profiles observed after in vitro treatment of MM cells with the respective drugs in the absence of BMSCs, providing direct molecular proof-of-principle of the ability of these recently developed anti-MM agents to counteract the protective effect of the BM milieu on MM cells. Furthermore, our studies not only shed light into the complex molecular phenomena of MM-BM milieu interactions, but also identify novel molecular pathways and targets that can also constitute novel therapeutic targets to improve the outcome of MM patients.

L5 ANSWER 14 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

AN 2003202378 EMBASE <<LOGINID::20070126>>

TI Dendritic cells genetically engineered to express IL-4 exhibit enhanced IL-12p70 production in response to CD40 ligation and accelerate organ allograft rejection.

AU Kaneko K.; Wang Z.; Kim S.H.; Morelli A.E.; Robbins P.D.; Thomson A.W.
CS A.W. Thomson, Department of Surgery, Univ. of Pittsburgh Medical Center, Thomas E. Starzl Transplant. Inst., 200 Lothrop St, Pittsburgh, PA 15213, United States

SO Gene Therapy, (2003) Vol. 10, No. 2, pp. 143-152.

Refs: 47

ISSN: 0969-7128 CODEN: GETHEC

CY United Kingdom

DT Journal; Article

FS 022 Human Genetics

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LA English

SL English

ED Entered STN: 29 May 2003

Last Updated on STN: 29 May 2003

AB C57BL/10 (B10; H2(b)) ***bone*** ***marrow*** -derived myeloid dendritic cells (DC) propagated in ***GM*** - ***CSF*** + IL-4 were transduced with r adenoviral (Ad) vectors encoding either control neomycin-resistance gene (Ad-Neo) or murine IL-4 (Ad-IL-4) on day 5 of culture following CD11c immunomagnetic bead purification. Both Ad-Neo- and Ad-IL-4-transduced DC displayed upregulated surface MHC class II and costimulatory molecules (CD40, CD80, CD86). Ad-IL-4 DC secreted higher levels of bioactive IL-12p70 after CD40 ligation or LPS stimulation than either Ad-Neo or unmodified DC. Only Ad-IL-4 DC produced IL-12p70 in primary MLR, in which they induced augmented proliferative responses of naive allogeneic C3H/HeJ (C3H; H2(k)) T-cells. Compared with Ad-Neo DC, Ad-IL-4 DC were also more effective in priming naive allogeneic recipients to exhibit specifically enhanced antitumor T-cell proliferative and CTL responses. T-cells primed in vivo 7 days previously with Ad-IL-4 DC displayed enhanced secretion of Th2 (IL-4, IL-10) but also higher Th1 cytokine (IFN. gamma.) production following ex vivo challenge with donor alloAg. Moreover, pretreatment of vascularized heart graft recipients with i.v. Ad-IL-4 DC, 1 week before transplant, significantly accelerated rejection and antagonized the therapeutic effect of anti-CD40L (CD154) mAb. These data contrast markedly with recently reported inhibitory effects of autologous Ad-IL-4 DC on autoimmune inflammatory disease.

L5 ANSWER 15 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:370255 CAPLUS <<LOGINID::20070126>>

DN 137:88524

TI Efficient mobilization and recruitment of marrow-derived endothelial and hematopoietic stem cells by adenoviral vectors expressing angiogenic factors

AU Rafil, S.; Heissig, B.; Hatton, K.

CS Division of Vascular Hematology-Oncology, Cornell University Medical College, New York, NY, 10021, USA

SO Gene Therapy (2002), 9(10), 631-641

CODEN: GETHEC; ISSN: 0969-7128

PB Nature Publishing Group

DT Journal; General Review

LA English

AB A review. Adult ***bone*** ***marrow*** (BM) is a rich reservoir for endothelial and hematopoietic stem and progenitor cells that contribute to revascularization of injured and tumor tissue. Physiol. stress results in the release of specific chemo-cytokines that promote mobilization of stem cells to the circulation and direct their incorporation into the target tissues. In order to dissect the mechanism and identify the cellular mediators that regulate stem cell recruitment, the authors have developed an in vivo murine model, in which the plasma levels of chemokines are elevated by introducing adenoviral vectors (Advectors) expressing such chemokines. Among the known stem cell-active chemokines, the angiogenic factor VEGF through interaction with its receptors, VEGFR2 and VEGFR1 expressed on endothelial and hematopoietic stem cells, promotes mobilization and recruitment of these cells into the neo-angiogenic sites, thereby accelerating the revascularization process. Based on these studies, it has become apparent that mobilization of stem cells is a dynamic process and requires sequential release of chemokines, expression of adhesion mol. and activation of proteases that facilitate egress of cells from the BM to the circulation. Chemokine-activation of metalloproteinases is essential for the release of bio-active cytokines, thereby enhancing stem cell mobilization potential. Advectors are ideal for delivery of chemokines since they allow for long-term robust expression facilitating in vivo proliferation and mobilization of large ***nos***. of an otherwise rare population of stem cells. VEGF-mobilized endothelial and hematopoietic stem cells provide for an enriched source of adult pluripotent cells that can be used for revascularization, tissue regeneration or gene therapy.

RE.CNT 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:118758 CAPLUS <<LOGINID::20070126>>

DN 137:332788

TI Long-term ***bone*** ***marrow*** culture-derived stromal

fibroblasts as a potential target for gene therapy in acute myelogenous leukemia

AU Min, Yoo Hong; Li, Guang Xun; Jang, Joon Ho; Suh, Hyung Chan; Kim, Jin Seok; Cheong, June Won; Lee, Seung Tae; Hahn, Jee Sook; Ko, Yun Woong
CS Department of Internal Medicine, Yonsei University College of Medicine, Seoul, 120-752, S. Korea

SO Leukemia Research (2002), 26(4), 369-376

CODEN: LEREDD; ISSN: 0145-2126

PB Elsevier Science Ltd.

DT Journal

LA English

AB As a part of our continuing efforts to develop gene therapy for acute myelogenous leukemia (AML), this study was undertaken to evaluate the possibility of using autologous ***bone*** ***marrow*** stromal fibroblasts (BMSFs) as a target cell population. Autologous BMSFs in AML were isolated from the stromal layers of long-term ***bone*** ***marrow*** culture (LTBM) using immunomagnetic beads. BMSFs exhibited rapid proliferation even in the absence of growth factors. Cultures stimulated with bFGF produced significantly increased ***nos***. of BMSFs than cultures without added growth factors. Using LNC/LacZ retroviral vector, the transduction efficiency of BMSFs was 13.+-4% at a 5 multiplicity of infection (MOI). LNC/interleukin-2 (IL-2)-transduced BMSFs produced between 1200 and 4800 pg of IL-2/106 cells per 24 h. Using ***adenoviral*** ***vector*** AdV/LacZ, the transduction efficiency was 84.+-10% at 100, and 92.+-8% at a MOI of 1000. Although the addn. of basic fibroblast growth factor, epidermal growth factor, or platelet-derived growth factor did not affect the transduction efficiency, they increased the ***nos***. of transduced cells significantly (P<0.01). AdV/IL-2-treated BMSFs produced high levels of IL-2 over the course of 7 days between 9820 and 22,700 pg of IL-2/106 cells per 24 h. Our finding that the genetically engineered autologous BMSFs of AML could be successfully established in vitro implies that BMSFs obtained from LTBM might be considered as a target cell population for certain types of clin. gene therapy in AML.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2002:579001 BIOSIS <<LOGINID::20070126>>

DN PREV200200579001

TI Regulation of HSC proliferation by homeobox transcription factors in engineered model systems.

AU Bjornsson, Jon Mar [Reprint author]; Brun, Ann; Larsson, Nina; Magnusson, Matias; Humphries, Keith; Karlsson, Stefan

CS Molecular Medicine and Gene Therapy, Lund University Hospital, Lund, Sweden

SO Blood Cells Molecules and Diseases, (May-June, 2002) Vol. 28, No. 3, pp. 332-333, print.

Meeting Info.: Third Conference on Stem Cell Gene Therapy: Biology and Technology, Rockville, MD, USA, March 21-23, 2002.

ISSN: 1079-9796.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 13 Nov 2002

Last Updated on STN: 13 Nov 2002

L5 ANSWER 18 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2002:443653 BIOSIS <<LOGINID::20070126>>

DN PREV200200443653

TI Sub-cutaneous injection of ***bone*** ***marrow*** derived dendritic cells engineered to produce interleukin-12 induces anti-tumor activities in an orthotopic mouse prostate cancer model.

AU Saika, Takashi [Reprint author]; Kusaka, Nobuyuki [Reprint author]; Satoh, Takefumi [Reprint author]; Mouraviev, Vladimir B. [Reprint author]; Yang, Guang [Reprint author]; Timme, Terry L. [Reprint author]; Thompson, Timothy C. [Reprint author]

CS Houston, TX, USA

SO Journal of Urology, (April, 2002) Vol. 167, No. 4 Supplement, pp. 54, print.

Meeting Info.: Annual Meeting of the American Urology Association, Inc. Orlando, Florida, USA, May 25-30, 2002.

CODEN: JOURAA; ISSN: 0022-5347.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 21 Aug 2002

Last Updated on STN: 21 Aug 2002

L5 ANSWER 19 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:507751 CAPLUS <<LOGINID::20070126>>

DN 135:103475

TI cDNA and protein sequence of fibroblast growth factor (***FGF***) sequence homolog zFGF12 and their uses in stimulation of mesenchymal cell proliferation

IN Conklin, Darrell C.

PA ZymoGenetics, Inc., USA

SO PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2001049740	A1	20010712	WO 2001-US238	20010104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2396401	A1	20010712	CA 2001-2396401	20010104
EP 1246843	A1	20021009	EP 2001-901722	20010104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518944	T	20030617	JP 2001-550280	20010104
PRAI US 2000-478062	A	20000105		
WO 2001-US238	W	20010104		

AB The present invention relates to polynucleotide and polypeptide mols. for zFGF12, a novel member of the "FGF" family. The present invention also includes antibodies to the zFGF12 polypeptides, and methods of using the polynucleotides and polypeptides to stimulating growth of cells from the mesenchymal lineage. The zFGF12 is mapped to chromosome 12(12p.1.3) and the tissue distribution of zFGF12 gene is described. The invention also provides the method to produce zFGF12 in E. coli, Pichia methanolica and chinese hamster ovary cells.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:489616 CAPLUS <<LOGINID::20070126>>

DN 135:88021

TI Combinations of silencer and inducible regulatory elements for tight regulation and strong induction of foreign genes in animal cells

IN Webster, Keith A.

PA University of Miami, USA

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001048187	A2	20010705	WO 2000-US33269	20001215
WO 2001048187	A3	20020530		
WO 2001048187	A9	20021107		

W: CA, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

US 6893867 B1 20050517 US 2000-723326 20001128

CA 2394174 A1 20010705 CA 2000-2394174 20001215

EP 1242592 A2 20020925 EP 2000-984041 20001215

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003523182 T 20030805 JP 2001-548700 20001215

PRAI US 1999-171597P P 19991223

US 2000-723326 A 20001128

WO 2000-US33269 W 20001215

AB Expression vectors are disclosed that are comprised of one or more silencer elements and conditionally inducible elements to form silencer-inducible regions and promoters in operative linkage upstream of at least one expressed region. The expression vector thereby regulates expression of at least one downstream region by conditional silencing in which an expressed DNA region of a gene is transcribed. Use of multiple copies of the silencer lowers the basal level of expression of the gene and therefore increases the induction ratio. Genetically engineered mammalian cells and non-human mammals can be made using such expression vectors through transfection and transgenesis techniques. Moreover, processes of making and using the aforementioned products are disclosed (e.g., the expression vector may be used diagnostically, therapeutically, or prophylactically). A series of constructs using repeats of the silencer element (SIL) of the human synapsin gene and the hypoxia response element (HRE) of the phosphoglycerate kinase gene were prep'd. and used to regulate expression of a luciferase reporter gene from the SV40 early promoter in animal cells. Induction of the reporter gene in hypoxic skeletal myocytes was directly proportional to the no. of copies of SIL/HRE pairs in the promoter region. The construct was more effective in skeletal myocytes than in cardiac myocytes. In a rat ischemic hindlimb model induction ratios for the reporter gene under ischemic (hypoxic) conditions was >20 for constructs carrying three copies of the SIL/HRE pairs. For animals carrying only three copies of the HRE element and no silencer elements the induction ratio was approx. 1.4.

L5 ANSWER 21 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:101291 CAPLUS <<LOGINID::20070126>>

DN 134:161880

TI cDNAs encoding the Flt-3 receptor ligand and there use as adjuvants in

vector vaccines

IN Hermanson, Gary George

PA Vical Inc., USA

SO PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2001009303	A2	20010208	WO 2000-US20679	20000731
WO 2001009303	A3	20010816		

W: CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-146170P P 19990730

AB A method of increasing the strength of the immune response of vector vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by administering in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

L5 ANSWER 22 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:851806 CAPLUS <<LOGINID::20070126>>

DN 136:1725

TI A novel fibroblast growth factor sequence homolog zFGF12

IN Conklin, Darrell C.

PA USA

SO U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 2001044525	A1	20011122	US 2001-754634	20010104
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US 2003180890	A1	20030925	US 2003-347505	20030117
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PRAI US 2000-174582P P 20000105

US 2001-754634 B1 20010104

AB The invention provides protein and cDNA sequences for a novel human fibroblast growth factor sequence homolog zFGF12, which has high sequence similarities with FGF19. The zFGF12 is mapped to chromosome 12 (12p.1.3) and the tissue distribution of zFGF12 gene is described. The invention also provides the method to produce zFGF12 in E. coli, Pichia methanolica and chinese hamster ovary cells. The present invention also includes antibodies to the zFGF12 polypeptides, and methods of using the polynucleotides and polypeptides to stimulating growth of cells from the mesenchymal lineage.

L5 ANSWER 23 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:365126 CAPLUS <<LOGINID::20070126>>

DN 135:135666

TI Infection of endothelium with E1-E4+, but not E1-E4-, adenovirus gene transfer vectors enhances leukocyte adhesion and migration by modulation of ICAM-1, VCAM-1, CD34, and chemokine expression

AU Rafii, Shahin; Dias, Sergio; Meeus, Sarah; Hattori, Koichi; Ramchandran, Ramalingam; Feuerback, Fred; Worgall, Stefan; Hackett, Neil R.; Crystal, Ronald G.

CS Division of Hematology-Oncology, Division of Pulmonary and Critical Care Medicine, Belfer Gene Therapy Core Facility, and Institute of Genetic Medicine, Cornell University Medical College, New York, NY, USA

SO Circulation Research (2001), 88(9), 903-910

CODEN: CIRUAL; ISSN: 0009-7330

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Intravascular introduction of replication-deficient adenoviral vectors (Advectors) provides an ideal model of delivery of transgenes for the treatment of various vascular abnormalities. On the basis of the knowledge that Advectors can induce inflammatory responses after intravascular administration, the authors speculated that cellular activation by Advector infection could directly modulate the endothelial cell (EC) adhesion mol./chemokine expression repertoire. Infection of human umbilical vein ECs or "bone" "marrow" microvascular ECs with an E1-E4+ Advector resulted in the up-regulation of intercellular adhesion mol.-1 (ICAM-1), vascular cell adhesion mol.-1 (VCAM-1), and CD34, but not E-selectin, P-selectin, CD36, CD13, CD44, HLA-DR or PECAM. Up-regulation of ICAM-1, VCAM-1, and CD34 was apparent 12 h after infection and persisted for weeks after infection. Selective induction of adhesion mols. was mediated by the presence of the E4 gene in the Advector, because infection of ECs with an E1-E4- Advector had no effect on adhesion mol. expression. ECs infected with E1-E4+ Advector, but not those infected with E1-E4- Advector, supported the adhesion of leukocytes. Monoclonal antibodies to ICAM-1 and VCAM-1 inhibited adhesion of leukocytes to E1-E4+ infected ECs. Infection of the ECs with E1-E4+ Advector, but not E1-E4- Advector, resulted in down-regulation of

expression of chemokines, including interleukin-8. ***MCP*** -
 *****, RANTES, and ***GM*** - ***CSF***. Nonetheless, a large
 no. of leukocytes migrated through ECs infected with E1-E4+, but not those
 infected with E1-E4-, in response to exogenous chemokines. These results
 demonstrate that infection of ECs with E1-E4+ Advectors, but not E1-E4-
 Advectors, may directly augment inflammatory responses by up-regulating
 expression of adhesion mols. and enhancing migration through
 Advector-infected ECs and suggest that E1-E4- Advectors may be a better
 choice for gene-transfer strategies directed to the ECs.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
 RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson
 Corporation on
 STN

AN 2002:220537 BIOSIS <<LOGINID::20070126>>

DN PREV200200220537

TI ***Bone*** ***marrow*** derived dendritic cell vaccination of
 spontaneous canine melanoma using human gp100 antigen. Clinical and
 immunological findings.

AU Gyorffy, Steve [Reprint author]; Woods, J. Paul; Foley, Ronan [Reprint
 author]; Kruth, Stephen; Liaw, Patricia C. Y. [Reprint author]; Gaudie,
 Jack [Reprint author]

CS Pathology and Molecular Medicine, McMaster University, Hamilton, ON,
 Canada

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 698a. print.
 Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
 Part 1, Orlando, Florida, USA, December 07-11, 2001. American Society of
 Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 3 Apr 2002

Last Updated on STN: 3 Apr 2002

AB Dendritic cells (DC) pulsed with tumor associated antigen (TAA) have
 emerged as promising candidates for therapeutic cancer vaccines by virtue
 of their ability to stimulate helper and cytotoxic T cell mediated
 anti-tumor responses. Canine oral melanoma, a spontaneous, highly
 metastatic neoplasia, which is resistant to conventional therapies may
 serve as an ideal candidate for DC based cancer immunotherapy. In this
 study, we demonstrate the ex vivo expansion and characterization of canine
 DC from unstimulated ***bone*** ***marrow***. These mature DC
 were transduced with an ***adenovirus*** (Ad) ***vector***
 expressing the human melanoma-associated antigen gp100 to vaccinate dogs
 diagnosed with primary, stage I, oral melanoma. ***Bone***
 marrow was obtained from three dogs, of various ages and breeds,
 under general anaesthesia during surgical resection of the primary tumor,
 and from a fourth healthy, control dog. ***Bone*** ***marrow***
 mononuclear cells were separated on a Ficoll gradient and cultured in RPMI
 1640 supplemented with 10% fetal bovine serum, and human recombinant
 cytokines ***GM*** - ***CSF*** (250 ng/ml), SCF (50 ng/ml), TNF (10
 ng/ml) and Flt-3 ligand (10ng/ml) for 12 days. Loosely adhered DC cell
 cultures were characterized by flow cytometric analysis for CD11c/CD18 and
 MHC-II cell surface expression using canine specific monoclonal antibodies
 at days 1 and 12 of culturing. Levels of CD11c/CD18 increased from 67% to
 98%, while MHC-II increased from 6% to 42% during this period. Electron
 microscopy showed that a majority of the cells had a phenotype consistent
 with DC cells. The cells were transduced on day 11 with Ad-2 gp100 at MOI
 150 for 24 hours using a similar protocol to that used in previous DC
 studies (Kaplan et al., J. Immunol. (1999), 163:699-707). Genetically
 modified DC were then re-injected subcutaneously into dogs on a schedule
 of three injections over 4 months with no side effects occurring.
 Peripheral blood cytotoxic T lymphocyte (CTL) activity was measured
 against autologous ***bone*** ***marrow*** stromal cells
 transfected with a plasmid encoding human gp 100 as target cells. A
 control and one tumor bearing dog demonstrated CTL activity. This dog has
 no clinical symptoms of recurrent melanoma 16 months after the initial
 injection, whereas the remaining two dogs showed no CTL activity and had
 recurrence or metastasis of the disease. This work demonstrates the
 feasibility of obtaining ***bone*** ***marrow*** derived DC for
 immunotherapeutic applications in outbred dogs developing spontaneous
 cancer. More significantly, these observations have direct relevance to
 human immunotherapy clinical trials and the measurement of clinical and
 immunological responses.

L5 ANSWER 25 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:707023 CAPLUS <<LOGINID::20070126>>

DN 133:261527

TI Intramyocardial injection of autologous ***bone*** ***marrow***
 for treatment of cardiac or myocardial conditions

IN Kornowski, Ran; Fuchs, Shmuel; Epstein, Stephen E.; Leon, Martin B.

PA USA

SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000057922	A1	20001005	WO 2000-US8353	20000330

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, US, UZ, VN, YU, ZW

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2368677	A1	20001005	CA 2000-2368677	20000330
EP 1171165	A1	20020116	EP 2000-919831	20000330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002540176	T	20021126	JP 2000-607671	20000330
AU 767402	B2	20031106	AU 2000-40452	20000330
US 7097832	B1	20060829	US 2001-868411	20010614
US 2004131601	A1	20040708	US 2003-618183	20030710
US 2004161421	A1	20040819	US 2004-776545	20040210
US 2006051334	A1	20060309	US 2005-117607	20050427
US 2006057722	A1	20060316	US 2005-221469	20050907
PRAI US 1999-126800P	P	19990330		
US 1999-138379P	P	19990609		
WO 2000-US8353	W	20000330		
US 2001-868411	A2	20010614		
US 2002-160514	A2	20020530		
US 2003-618183	A2	20030710		
US 2004-566332P	P	20040428		
US 2004-608272P	P	20040908		

AB A method of treating cardiac or myocardial conditions comprises the
 administration of an effective amt. of autologous ***bone***
 marrow. The ***bone*** ***marrow*** may optionally be
 stimulated and/or administered in combination with a pharmaceutical drug,
 protein, gene, or other factor or therapy that may enhance ***bone***
 marrow prodn. of angiogenic growth factors and/or promote
 endothelial cell proliferation or migration or blood vessel formation.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:190960 CAPLUS <<LOGINID::20070126>>

DN 132:235909

TI In situ injection of antigen-presenting cells with genetically enhanced
 cytokine expression

IN Tahara, Hideaki; Lotze, Michael T.; Nishioka, Yasuhiko

PA University of Pittsburgh of the Commonwealth System of Higher Education,
 USA

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000015264	A1	20000323	WO 1999-US21097	19990914
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2343355	A1	20000323	CA 1999-2343355	19990914
AU 9961444	A1	20000403	AU 1999-61444	19990914
EP 1113821	A1	20010711	EP 1999-948217	19990914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002524537	T	20020806	JP 2000-569848	19990914
PRAI US 1998-100468P	P	19980915		
WO 1999-US21097	W	19990914		

AB The use of professional antigen presenting cells genetically modified to
 enhance expression of an immunostimulatory cytokine is disclosed for the
 treatment of individuals having tumors or infections. The genetically
 modified professional antigen presenting cells are injected directly at or
 near the site of the tumor or infection. Preferred professional antigen
 presenting cells include dendritic cells, and preferred immunostimulatory
 cytokines include interleukins such as IL-12.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
 RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
 reserved on STN

AN 2000112930 EMBASE <<LOGINID::20070126>>

TI Transgenic expression of granulocyte-macrophage colony-stimulating factor
 induces the differentiation and activation of a novel dendritic cell
 population in the lung.

AU Wang J.; Snider D.P.; Hewlett B.R.; Lukacs N.W.; Gaudie J.; Liang H.;
 Xing Z.

CS Z. Xing, Health Sciences Centre, Dept. of Pathol. and Molec. Medicine,
 McMaster University, Hamilton, Ont. L8N 3Z5, Canada.
 xingz@fhs.cmu.mcmaster.ca

SO Blood, (1 Apr 2000) Vol. 95, No. 7, pp. 2337-2345.

Refs: 46
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry

LA English
SL English
ED Entered STN: 13 Apr 2000
Last Updated on STN: 13 Apr 2000

AB The role of granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***) in the differentiation of dendritic cells (DCs) during pulmonary viral infection was investigated by using a mouse model of ***GM*** - ***CSF*** transgene expression established with an ***adenoviral*** vector*** (AdGM-CSF). ***GM*** - ***CSF*** gene transfer resulted in increased levels of ***GM*** - ***CSF*** in the lung, which peaked at day 4 and remained increased up to day 19. A striking cellular response composed predominantly of macrophage-like cells was observed in the lung receiving AdGM-CSF but not control vector. By FACS analysis, the majority of these cells were identified at an early time point as macrophages and later as mature/activated myeloid DCs characterized by CD11b(bright), CD11c(bright), MHC class II(bright), and B7.1(bright). In contrast, ***GM*** - ***CSF*** had a weak effect on a small DC population that was found present in normal lung and was characterized by CD11c(bright) and CD11b(low). By immunohistochemistry staining for MHC II, the majority of activated antigen-presenting cells were localized to the airway epithelium and peribronchial/perivascular areas in the lung. A concurrently enhanced Th1 immune response was observed under these conditions. The number of CD4 and CD8 T cells was markedly increased in the lung expressing ***GM*** - ***CSF***, accompanied by increased release of interferon (IFN).gamma. in the lung. Furthermore, lymphocytes isolated from either lung parenchyma or local draining lymph nodes of these mice but not the control mice released large amounts of IFN.gamma. on adenoviral antigen stimulation in vitro. These findings reveal that ***GM*** - ***CSF*** promotes the differentiation and activation of a myeloid DC population primarily by acting on macrophages during pulmonary immune responses. (C) 2000 by The American Society of Hematology.

L5 ANSWER 28 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

AN 2000:279348 BIOSIS <<LOGINID::20070126>>
DN PREV200000279348

TI Comparative analysis of genetically modified dendritic cells and tumor cells as therapeutic cancer vaccines.

AU Klein, Christoph; Bueler, Hansruedi; Mulligan, Richard C. [Reprint author]
CS Howard Hughes Medical Institute, Children's Hospital, 320 Longwood Ave., Enders 861, Boston, MA, 02115, USA

SO Journal of Experimental Medicine, (May 15, 2000) Vol. 191, No. 10, pp. 1699-1708. print.
CODEN: JEMEAU. ISSN: 0022-1007.

DT Article
LA English
ED Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB We have directly compared the efficacy of two immunotherapeutic strategies for the treatment of cancer: "vaccination" of tumor-bearing mice with genetically modified dendritic cells (DCs), and vaccination with genetically modified tumor cells. Using several different preexisting tumor models that make use of B16F10 melanoma cells expressing a target tumor antigen (human melanoma-associated gene (MAGE)-1), we found that vaccination with ***bone*** marrow*** -derived DCs engineered to express MAGE-1 via adenoviral-mediated gene transfer led to a dramatic decrease in the number of metastases in a lung metastasis model, and led to prolonged survival and some long-term cures in a subcutaneous preexisting tumor model. In contrast, vaccination with granulocyte/macrophage colony-stimulating factor (***GM*** - ***CSF***)-transduced tumor cells, previously shown to induce potent antitumor immunity in standard tumor challenge assays, led to a decreased therapeutic effect in the metastasis model and no effect in the subcutaneous tumor model. Further engineering of DCs to express either ***GM*** - ***CSF***, tumor necrosis factor alpha, or CD40 ligand via retroviral-mediated gene transfer, led to a significantly increased therapeutic effect in the subcutaneous tumor model. The immunological mechanism, as shown for ***GM*** - ***CSF*** -transduced DCs, involves MAGE-1-specific CD4+ and CD8+ T cells. Expression of ***GM*** - ***CSF*** by DCs led to enhanced cytotoxic T lymphocyte activity, potentially mediated by increased numbers of DCs in draining lymph nodes. Our results suggest that clinical studies involving the vaccination with genetically modified DCs may be warranted.

L5 ANSWER 29 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2000:131423 EMBASE <<LOGINID::20070126>>

TI Local and systemic effects after adenoviral transfer of the murine granulocyte-macrophage colony-stimulating factor gene into mice.

AU Burger J.A.; Baird S.M.; Powell H.C.; Sharma S.; Eling D.J.; Kipps T.J.
CS Dr. J.A. Burger, Department of Medicine, Division of Hematology/Oncology, University of California, 9500 Gilman Drive, San Diego, CA 92093-0663, United States. jtburger@ucsd.edu

SO British Journal of Haematology, (2000) Vol. 108, No. 3, pp. 641-652.

Refs: 41
ISSN: 0007-1048 CODEN: BJHEAL
CY United Kingdom
DT Journal; Article
FS 022 Human Genetics
025 Hematology
037 Drug Literature Index

LA English
SL English
ED Entered STN: 27 Apr 2000
Last Updated on STN: 27 Apr 2000

AB Vectors encoding immunostimulatory genes are under investigation for their use as adjuvants for immunotherapy. Granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***) is a prominent candidate gene for this approach because this cytokine can prime immune responses to 'self' tumour or other weak antigens. Prior studies suggested that ***GM*** - ***CSF*** induces accumulation and differentiation of antigen-presenting cells, particularly dendritic cells that can initiate immunity. To evaluate this model in vivo, we performed i.m. and i.p. injections of an ***adenovirus*** vector*** encoding murine ***GM*** - ***CSF*** (Ad-mGM-CSF) and evaluated local and systemic effects. After intramuscular injection, local changes were characterized by the accumulation of myeloid cells, a subsequent infiltration of lymphocytes and then myonecrosis. Intraperitoneal injection also induced an accumulation of myeloid cells, an increase in CD3+ positive T and a decrease in B220-positive B lymphocytes. Expression of the dendritic cell marker CD11c on 48 +/- 9% of the peritoneal cells (n = 6) along with high levels of surface MHC class II, a characteristic morphology, and endocytosis of FITC-dextran suggested in vivo differentiation of dendritic cells after i.p. injection of Ad-mGM-CSF. Systemic effects were observed after i.m. and i.p. injection of Ad-mGM-CSF. All mice developed hepatosplenomegaly resulting from extramedullary haematopoiesis. These changes were specific to ***GM*** - ***CSF*** as they were not seen in mice injected with an ***adenovirus*** vector*** without a transgene. Our observations indicate that adenoviral transfer of ***GM*** - ***CSF*** is a powerful tool for inducing local and systemic expansion of haematopoietic cells. The local expansion of myeloid cells displaying signs of dendritic cell differentiation, as characterized for the peritoneal cell compartment, can explain the potency of ***GM*** - ***CSF*** when used as an adjuvant in genetic immunotherapy.

L5 ANSWER 30 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

AN 2001:311471 BIOSIS <<LOGINID::20070126>>
DN PREV200100311471

TI Enhanced hematopoietic recovery after coinfection of hematopoietic stem cells and ***bone*** marrow*** stromal cells which were transfected with ***adenoviral*** vector*** carrying the ***GM*** - ***CSF*** gene in a mouse BMT model.

AU Kim, Hyo Jung [Reprint author]; Kim, Sang-Hee [Reprint author]; Suh, Cheolwon [Reprint author]; Kim, Sung Bae [Reprint author]; Park, Jung Sun; Cho, Hwa Jeong; Lee, Jung Shin [Reprint author]; Kim, Woo Kun [Reprint author]

CS Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 387b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology, San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB The ***bone*** marrow*** mesenchymal stem cells are a heterogeneous population. The proliferation of hematopoietic stem cells and their differentiation occurs in association with stromal cells as well as the cytokines and extracellular matrix components produced by the stromal cells. The use of cultured stromal cells as a vehicle for cell or gene therapy is an attractive method for rapid engraftment after BMT. The aims of this study was to evaluate the effects of coinfecting BM stromal cells which were transfected with ***adenoviral*** vector*** carrying the ***GM*** - ***CSF*** gene on hematopoietic engraftment in a mouse BMT model. C3H strain mice (male, 8 weeks old) were irradiated (8.5Gy) and infused with BM stem cells (5*10⁵) via ophthalmic vein. MS-5 cells (mouse BM stromal cell line) were transfected with recombinant adenovirus carrying mouse ***GM*** - ***CSF*** (Adv-GMCSF, 50M.O.I) or E1 region deleted adenovirus (DELTA-E1-Adv). Experiment was divided with 3 groups: coinfection of A) BM stem cells + control MS-5 cells (5*10⁶), B) BM stem cells + MS-5 cells transfected with DELTA-E1-Adv and C) BM stem cells + MS-5 cells transfected with Adv-GMCSF. On day 14 after BMT, mice were sacrificed and their spleens were examined for CFUS (colony forming units in spleen) assay. BM cells were obtained by flushing femurs and tibias, culture for CFUC (colony forming units in culture) assay was done for 2 weeks. To confirm the engraftment of MS-5 cells in tissues, total cellular RNA was extracted from BM, spleen and liver for RT-PCR (adenovirus type 5 CMV region and ***GM*** - ***CSF***). The number of mice were 3 at each study group. Transfection efficiency of Adv-GMCSF at 50 M.O.I on MS-5 was 60%. By RT-PCR, expected

bands of the PCR product were observed in MS-5 cells-Adv-GMCSF, BM, spleen, liver extracts. The colony counts of CFUC assay were significantly higher in group C (A : B : C = 5.8 : 1 : 18.5) In group C, the colony size is larger and fibroblast-like stromal cells were found under the colony formations. CFUS showed increased and packed with primitive progenitor cells in group C. In this study we found that BM stromal cells are efficient vehicles for transfection of adenovirus carrying the ***GM*** - ***CSF*** gene and they have an ability to home into the ***bone*** ***marrow***. Coinfused MS-5cells - Adv-GMCSF can accelerate the ability of the hematopoietic recovery in a mouse BMT model.

L5 ANSWER 31 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:321975 BIOSIS <<LOGINID::20070126>>
DN PREV200100321975
TI Transient over expression of HoxB4 in human CD34+ umbilical cord blood cells by adenovirus leads to differentiation in vitro.
AU Brun, Ann [Reprint author]; Fan, Xiaolong [Reprint author]; Karlsson, Stefan [Reprint author]
CS Department of Molecular Medicine and Gene Therapy, Lund University, Lund, Sweden
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 210a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
AB The transcription factor HoxB4 is normally expressed in primitive hematopoietic cells and is down regulated as the cells mature and differentiate. Over expression of the transcription factor HoxB4 in murine ***bone*** ***marrow*** cells transplanted into irradiated recipients caused increased proliferation of the most primitive hematopoietic cells in vivo. We wanted to ask whether transient overexpression of HoxB4 would increase proliferation of primitive hematopoietic stem cells to facilitate gene transfer by oncoretroviral vectors. We constructed a recombinant adenovirus expressing the transcription factor HoxB4 together with the enhanced green fluorescent protein (eGFP), each under the control of the hCMV promoter. As a negative control an ***adenoviral*** ***vector*** containing the eGFP gene alone, was used. Adenoviral transduction efficiency, proliferation and viability were studied in human CD34+ cord blood cells. Transduced eGFP sorted cells were plated in single cell assays and grown in serum free medium with various cytokine combinations. Both control and HoxB4 containing vectors transduced 10-30% of the CD34+ cells. With low cytokine support (megakaryocyte growth and development factor (MGDF) or c-kit ligand (KL) alone) in a single cell assay HoxB4 transduced cells proliferated poorly (18.5% +/- 10.3% and 28.1% +/- 8.5% respectively) compared to control cells (42.6% +/- 12.6% and 60.7% +/- 14.7% respectively). In combination of MGDF, KL and Flt3 ligand (FL) the difference was less pronounced but still present (66.0% +/- 2.7% for HoxB4 transduced cells and 76.7% +/- 4.6% for control cells). When MGDF, KL and FL were combined with erythropoietin (Epo) the HoxB4 cells increased their survival to 93.4% +/- 3.6%, while control cells increased to 84.2% +/- 8.9%. Further analysis of the HoxB4-transduced cells showed that over expression of HoxB4 induce differentiation with an increase in myeloid cells (CD14, CD15) from 6.3% +/- 1.6% to 28.0% +/- 1.8% (p=0.037), and erythroid cells (GpA) from 1.5% +/- 1.4% to 13.4.0% +/- 6.1% (p=0.034) determined by FACS analysis after 5 days of culture in MGDF, KL, FL and Epo. Study of CFU-C with stimulation towards erythrocyte (SCF + Epo) or myeloid cell formation (IL-3 + ***GM*** - ***CSF***) is under investigation. Therefore, HoxB4 over expression in CD34+ UCB cells in vitro causes differentiation rather than proliferation.

L5 ANSWER 32 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:468817 CAPLUS <<LOGINID::20070126>>
DN 133:191857
TI CTLA4lg inhibits T cell-dependent B-cell maturation in murine systemic lupus erythematosus
AU Mihara, Masahiko; Tan, Irene; Chuzhin, Yelena; Reddy, Bhoompally; Budhai, Lalbachan; Holzer, Aton; Gu, Yun; Davidson, Anne
CS Department of Medicine, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SO Journal of Clinical Investigation (2000), 106(1), 91-101
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal
LA English
AB Long-term administration of CTLA4lg prevents the onset of disease in systemic lupus erythematosus-prone (SLE-prone) NZB/NZW F1 mice. To detect the mechanism of this effect, the authors engineered an adenovirus that expresses murine CTLA4lg. Administration of a single high dose of this virus results in long-term expression of CTLA4lg in the serum and absence of an immune response to the ***adenoviral*** ***vector***. The authors administered Ad-CTLA4lg to 19- to 22-wk-old NZB/NZW F1 mice and evaluated the effect on anti-DNA antibody-producing B cells. The authors show that CTLA4lg has a beneficial effect on murine SLE for as long as it is present in the serum. This effect is associated with decreased expansion

of both the IgM and IgG autoreactive B-cell population, inhibition of Ig class switching, decreased frequency and altered pattern of somatic mutation, and a marked decrease in the ***nos*** of activated CD4-pos. T cells. In contrast, intrinsic B-cell hyperactivity and the survival of plasma cells in the ***bone*** ***marrow***, both of which are less dependent on T-cell help, appear to be unaffected by CTLA4lg. High-dose CTLA4lg did not induce permanent tolerance in this autoimmune disease model. Furthermore, although the mice survived in a conventional housing facility, treatment with Ad-CTLA4lg was immunosuppressive.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:764169 CAPLUS <<LOGINID::20070126>>
DN 132:9605
TI Expansion of hematopoietic stem cells transduced with mdr-1 and methods and therapeutic applications
IN Sorrentino, Brian; Bunting, Kevin
PA St. Jude Children's Research Hospital, USA
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 9961589 A2 19991202 WO 1999-US11825 19990527
WO 9961589 A3 20000127
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9942147 A 19991213 AU 1999-42147 19990527
US 6933150 B1 20050823 US 2000-584586 20000531
US 2002102244 A1 20020801 US 2001-866866 20010529
PRAI US 1998-86988P P 19980528
WO 1999-US11825 W 19990527
US 2000-584586 A2 20000531
AB The present invention includes methods of performing ex vivo expansion of gene-modified hematopoietic stem cells which are useful for many applications involving ***bone*** ***marrow*** transplantation and ex vivo gene therapy. The present invention further includes the gene-modified hematopoietic stem cells that are used and produced by such methods. Such gene-modified hematopoietic stem cells can also contain a second heterologous gene. This may include an early-acting hematopoietic cytokines which includes interleukin-3, interleukin-6, G-CSF, ***GM*** - ***CSF***, FLT-3 ligand, and stem cell factor. In addition, the present invention also includes methods of engrafting the gene-modified hematopoietic stem cells of the present invention into animals, including for ex vivo gene therapy and for reconstitution of hematopoietic cells in ablated mammals. Viral vectors were utilized in these studies for effective expression. The expansion of cells capable of long-term engraftment in a non-irradiated mouse model was unexpected.

L5 ANSWER 34 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:595358 CAPLUS <<LOGINID::20070126>>
DN 131:223487
TI Induction of apoptotic or cytotoxic gene expression by adenovirus-mediated gene delivery
IN McDonnell, Timothy J.; Swisher, Stephen G.; Fang, Bingliang; Bruckheimer, Elizabeth M.; Sarkiss, Mona G.; Ji, Li; Roth, Jack A.
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 9946371 A2 19990916 WO 1999-US5359 19990311
WO 9946371 A3 20000824
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2322663 A1 19990916 CA 1999-2322663 19990311
AU 9931837 A 19990927 AU 1999-31837 19990311
AU 762493 B2 20030626
EP 1070122 A2 20010124 EP 1999-913854 19990311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
US 6899870 B1 20050531 US 1999-266465 19990311

US 2006002895 A1 20060105 US 2005-141678 20050531
PRAI US 1998-77541P A2 19980311
US 1999-266465 A3 19990311
WO 1999-US5359 W 19990311

AB The present invention relates to adenoviral vectors contg. propapoptotic genes of the Bcl-2 gene family and their use in cancer therapy. The vector may addnl. contain a second gene, e.g., one encoding a tumor suppressor, a cytokine, a receptor, a differentiating agent, or a nucleic acid antisense to an oncogene. Thus, ***adenoviral*** ***vector*** Ad-Bax, contg. a truncated Bax gene encoding a Bax protein contg. an intact BH3 death domain, induced apoptosis in human breast cancer cells.

L5 ANSWER 35 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:297332 CAPLUS <<LOGINID::20070126>>

DN 130:320854

TI Use of genetic vectors as vehicles for genetic information enabling mammalian cells to produce agents for the treatment of bone pathologies

IN Baltzer, Axel Wilhelm August; Lattermann, Christian; Whalen, Janey Desales; Robbins, Paul David; Evans, Christopher Howard

PA Germany

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921589	A2	19990506	WO 1998-EP6849	19981029
WO 9921589	A3	19991014		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LU, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19747718	A1	19990506	DE 1997-19747718	19971029
DE 19747719	A1	19990512	DE 1997-19747719	19971029
CA 2308511	A1	19990506	CA 1998-2308511	19981029
AU 9915579	A	19990517	AU 1999-15579	19981029
AU 750803	B2	20020725		
EP 1027076	A2	20000816	EP 1998-959810	19981029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 7105494	B1	20060912	US 2000-561524	20000428
US 2006099182	A1	20060511	US 2005-300698	20051214
PRAI DE 1997-19747718	A	19971029		
DE 1997-19747719	A	19971029		
WO 1998-EP6849	W	19981029		
US 2000-561524	A1	20000428		

AB Vectors such as recombinant adenoviruses, adeno-assocd. viruses, retroviruses, herpes simplex viruses, liposomes, and plasmids are useful as agents which stimulate mammalian cells to produce therapeutic proteins that act on a cellular level for genetic treatment of bone pathologies such as osteoporosis and loss of bone mass, as well as to promote the incorporation of bone, ligament, and tendon transplants. The vectors may be administered parenterally, intraosteally, or locally to the site of bone pathol., or may be used to treat the patient's cells ex vivo followed by autologous reimplantation. They may contain cDNA for bone morphogenetic proteins 2-7, TGF-beta., ***FGF***, IGF, PDGF, vascular endothelial growth factor, cytokines, cytokine inhibitors, or marker proteins. Thus, ovariectomy-induced bone loss in 6-wk-old mice, which results from osteoclast activation by elevated systemic levels of interleukin 1 and TNF-alpha., was approx.50% diminished by systemic gene therapy with an ***adenovirus*** ***vector*** encoding interleukin 1 receptor antagonist protein.

L5 ANSWER 36 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson

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STN

DUPLICATE 2

AN 2000:11432 BIOSIS <<LOGINID::20070126>>

DN PREV200000011432

TI Adenovirus-mediated transfer of HST-1/ ***FGF*** -4 gene protects mice from lethal irradiation.

AU Takahama, Yasushi; Ochiya, Takahiro; Tanooka, Hiroshi; Yamamoto, Hanako;

Sakamoto, Hiromi; Nakano, Hiroshige; Terada, Masaaki [Reprint author]

CS National Cancer Center, 1-1 Tsukiji, 5-chome Chuo-ku, Tokyo, 104-0045, Japan

SO Oncogene, (Oct. 21, 1999) Vol. 18, No. 43, pp. 5943-5947. print.

CODEN: ONCNES. ISSN: 0950-9232.

DT Article

LA English

ED Entered STN: 23 Dec 1999

Last Updated on STN: 31 Dec 2001

AB Intraperitoneal injection of a replication-deficient adenovirus containing the HST-1 (***FGF*** -4) gene (Adex1HST-1) increased peripheral platelet counts in mice, and also effectively prevented experimentally induced thrombocytopenia. Here, we report the therapeutic potential of Adex1HST-1 on severely injured mice after exposure to otherwise lethal irradiation. Eighteen out of 20 mice that received Adex1HST-1 prior to gamma-irradiation (9 Gy) survived, while all the 20 mice with prior administration of control adenoviruses died after irradiation (P<0.0001).

Hematological and histopathological analyses revealed that Adex1HST-1 acts as a potent protector against lethal irradiation, which causes injury of intestinal tract as well as myelosuppression in the ***bone***

marrow and spleen. These data demonstrate that the protective effects of administration of Adex1HST-1 against irradiation are superior to any other protective effects of cytokines against a lethal dose of irradiation, and that the pre-administration of Adex1HST-1 may be useful for lessening the side effects of currently used chemo- and radio-therapy against cancer.

L5 ANSWER 37 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:185625 CAPLUS <<LOGINID::20070126>>

DN 131:17653

TI Transduction of dendritic cells with adenoviral vectors encoding CTLA4-Ig markedly reduces their allostimulatory activity

AU Lu, L.; Lee, W.-C.; Gambotto, A.; Zhong, C.; Robbins, P. D.; Qian, S.; Fung, J. J.; Thomson, A. W.

CS Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, 15213, USA

SO Transplantation Proceedings (1999), 31(1/2), 797

CODEN: TRPPA8; ISSN: 0041-1345

PB Elsevier Science Inc.

DT Journal

LA English

AB Mature dendritic cells (DC) are potent antigen-presenting cells (APC). However, immature DC lacking sufficient expression of cell surface costimulatory mol. can induce alloantigen-specific T-cell anergy in vitro and prolong cardiac allograft survival. However they do not induce permanent allograft acceptance in non-immunosuppressed recipients. The failure of these cells to induce allograft tolerance may be due to the "late" upregulation of costimulatory mol. on the DC following their interaction with host T cells. This explanation is supported by the observation that coculture of costimulatory mol.-deficient DC with allogeneic T cells for 18 h induces CD40 and B7 mol. expression on the DC. In this study the authors hypothesized that DC transduced with genes encoding CTLA4-IgA potent blocking protein of the B7-CD28 costimulatory pathway might enhance their tolerogenicity. DC were transduced efficiently by Ad-LacZ or Ad-EGFP (the transduction rates were 86,83 78 and 76% at 100,50 20 and 10 MOI resp.). Ad-LacZ or Ad-EGFP transduction did not influence costimulatory mol. expression, allostimulatory activity, CTL induction, DC migration pattern and survival in allogeneic hosts. However survival of Ad-CTLA4-Ig-transduced DC was enhanced in allogeneic recipients as DC transduced with Ad-CTLA4-Ig were detected in four to fivefold increased ***nos*** in the spleen compared to those transduced with Ad-LacZ or non-transduced DC 7 days after injection in C3H mice. DC transduced with Ad-CTLA4-Ig exhibited a striking redn. in staining for CD86 (B7-2) but not MHC class II and became poor stimulators of T-cell proliferation and CTL responses. The supernatant from Ad-CTLA4-Ig-transduced DC significantly inhibited naive C3H T-cell proliferation stimulated by unmodified B10 mature DC suggesting the prodn. of functional CTLA4-Ig by the Ad-CTLA4-Ig-transduced DC. Moreover Ad-CTLA4-Ig-transduced DC induced alloantigen-specific T-cell hyporesponsiveness since C3H T cells cocultured with B10 Ad-CTLA4-Ig DC were significantly impaired in their responses to subsequent restimulation by splenic APC from B10 mice but not from a third party. These data indicate that ***bone*** ***marrow*** -derived DC can be transduced efficiently and modified functionally with Ad-CTLA4-Ig and that CTLA4-Ig-transduced DC exhibit markedly impaired alloimmunostimulatory activity and capacity to induce CTL responses. Moreover CTLA4-Ig-transduced DC show potential for the induction of alloantigen-specific T-cell hyporesponsiveness and enhanced survival in allogeneic hosts. These genetically engineered DC may be of value for the therapy of allo or autoimmune.

RE CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN

DUPLICATE 3

AN 1999:300792 BIOSIS <<LOGINID::20070126>>

DN PREV199900300792

TI Recombinant adenovirus vectors for cytokine gene therapy in mice.

AU Kurata, Hirokazu; Liu, Chang-Bai; Valkova, Joulieta; Koch, Alisa E.;

Yssel, Hans; Hirabayashi, Yoko; Inoue, Tohru; Yokota, Takashi; Arai,

Ken-ichi [Reprint author]

CS Department of Molecular and Developmental Biology, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo, 108, Japan

SO Journal of Allergy and Clinical Immunology, (May, 1999) Vol. 103, No. 5

PART 2, pp. S471-S484. print.

CODEN: JACIBY. ISSN: 0091-6749.

DT Article

LA English

ED Entered STN: 12 Aug 1999

Last Updated on STN: 12 Aug 1999

AB Background: Adenoviruses have several specific features useful for gene therapy. They infect various lineages of cells irrespective of cell cycle status. However, the exact mechanism of their infection and in vivo kinetics as a gene expression vector have not been elucidated. Objective: Using adenovirus vectors expressing marker genes, we examined the infectivity of these vectors (including cellular and tissue tropism), the duration and intensity of transgene expression, and the side effects.

Methods: Various cells were infected with adenovirus expressing LacZ gene at various doses, and beta-galactosidase activity was measured and compared in relation with dose, time course, and cellular vitronectin receptor. Mice were injected with adenoviruses expressing LacZ, luciferase and ***GM*** - ***CSF***, and in vivo gene expression was examined. Results: Adenovirus infection induced viral dose-dependent transgene expression that persisted for 2 weeks. Adherent cells were infected much more efficiently than nonadherent cells, probably because the former expressed much higher levels of the vitronectin receptor, one of the main receptors for adenovirus. Studies performed in mice with luciferase-expressing adenovirus revealed that the liver was the main target organ after intravenous injection and showed that the intravenous route was superior to other routes with regard to transgene expression. After intravenous injection of adenovirus expressing human ***GM*** - ***CSF***, there was a transient and dose-dependent increase in the serum level of this cytokine. Administration of adenovirus expressing mouse ***GM*** - ***CSF*** enhanced hematopoiesis in the spleen and ***bone*** ***marrow***. Conclusion: These results indicated that adenoviruses can be used for in vivo cytokine gene therapy but suggested the necessity of taking into consideration the route of administration, the duration of transgene expression, the toxic dose, and host immune reactions.

L5 ANSWER 39 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:247206 CAPLUS <<LOGINID:20070126>>
DN 131:101197
TI In vivo migration and survival of donor-derived dendritic cell progenitors genetically modified using an ***adenoviral*** ***vector*** encoding cDNA for TGF beta.1
AU Zhong, Cuiping; Li, Weizhen; Lu, Lina; Qian, Shiguang; Thomson, Angus W.
CS Department of Histology and Embryology, Shanghai Medical University, Shanghai, 200032, Peop. Rep. China
SO Zhonghua Yixue Zazhi (1999), 79(3), 174-177
CODEN: CHHTAT; ISSN: 0376-2491
PB Zhonghua Yixue Zazhi
DT Journal
LA Chinese
AB The migration and survival of B10 mouse ***bone*** ***marrow*** (BM)-derived DCs in C3H mice and whether genetic modification of these DCs to overexpress TGFVb1 may potentiate their tolerogenicity were studied. B10 mouse BM-derived DCs were propagated in ***GM*** - ***CSF*** and TGFVb (DC1), then DC1 was transduced with replication-deficient Ad vectors encoding genes for LacZ (DC2) or TGFVb1 (DC3). Cells of different groups were injected into 1 footpad of C3H mice. The mice were sacrificed on days 1, 2, 7, and 14, and spleens, thymuses, popliteal and mesenteric lymph nodes (LN) were removed and stained with anti-IAb mAb. The incidences of B10 DC were detd. by the mean no. of IAb pos. cells with dendritiform morphol. per low power field (x 100). Transduction with Ad-LacZ or Ad-TGFVb1 did not affect DC migration or distribution in C3H recipients, i. e. IAb+ cells were first obsd. under the capsule of popliteal LN (peak at d1), then migrated into the marginal T dependent area of spleens (peak at d7), and were found occasionally in the thymus. Transduction of Ad-LacZ reduced the ***nos*** of IAb+ cells identified in both LN and spleens at all time points post injection, compared with injection of unmodified control DC, suggesting that Ad transduction itself can affect DC life span in allogeneic recipients. Overexpression of TGFVb1 by transduction of Ad- TGFVb1 not only fully reversed the redn. of DC ***nos*** induced by Ad transduction, but also prolonged the life span of DC in spleen, as shown by the 2-fold increase in no. of IAb+ cells in spleen at d14 compared with control DCs. Mouse BM-derived TGFVbDCs can be transduced to express TGFVb1 using an ***adenoviral*** ***vector***, and exhibit the same migration characteristics as unmodified DC. The survival of TGFVb gene transduced DCs appears to be enhanced compared with unmodified or LacZ gene-transduced DCs.

L5 ANSWER 40 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2000:45770 BIOSIS <<LOGINID:20070126>>
DN PREV200000045770
TI Thrombopoietin adenovector-transfected OP-9 cells support long term human hematopoiesis in vitro.
AU Feugier, P. [Reprint author]; Jo, D. Y. [Reprint author]; Shieh, J. H. [Reprint author]; Hackett, N. R. [Reprint author]; Crystal, R. G. [Reprint author]; Moore, M. A. S. [Reprint author]
CS Sloan-Kettering Institute for Cancer Research, Weill Medical College of Cornell University, New York, NY, USA
SO Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 42a. print. Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology, New Orleans, Louisiana, USA. December 3-7, 1999. The American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 26 Jan 2000
Last Updated on STN: 31 Dec 2001

L5 ANSWER 41 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:324116 CAPLUS <<LOGINID:20070126>>

DN 129:76454
TI High-efficiency myogenic conversion of human fibroblasts by ***adenoviral*** ***vector*** -mediated MyoD gene transfer
AU Lattanzi, Laura; Salvatori, Giovanni; Coletta, Marcello; Sonnino, Claudia; De Angelis, M. Gabriella Cusella; Gioglio, Luciana; Murry, Charles E.; Kelly, Robert; Ferrari, Giuliana; Molinaro, Mario; Crescenzi, Marco; Mavillo, Fulvio; Cossu, Giulio
CS Department of Histology of Medical Embryology, Univ. di Roma La Sapienza, Rome, 00161, Italy
SO Journal of Clinical Investigation (1998), 101(10), 2119-2128
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB Ex vivo gene therapy of primary myopathies, based on autologous transplantation of genetically modified myogenic cells, is seriously limited by the no. of primary myogenic cells that can be isolated, expanded, transduced, and reimplanted into the patients muscles. We explored the possibility of using the MyoD gene to induce myogenic conversion of nonmuscle, primary cells in a quant. relevant fashion. Primary human and murine fibroblasts from skin, muscle, or ***bone*** ***marrow*** are infected by an E1-deleted ***adenoviral*** ***vector*** carrying a retroviral long terminal repeat-promoted MyoD cDNA. Expression of MyoD caused irreversible withdrawal from the cell cycle and myogenic differentiation in the majority (from 60 to 90%) of cultured fibroblasts, as defined by activation of muscle-specific genes, fusion into contractile myotubes, and appearance of ultrastructurally normal sarcomeres in culture. 24 H after adenoviral exposure, MyoD-converted cultures were injected into regenerating muscle of immunodeficient (severe combined immunodeficiency/beige) mice, where they gave rise to .beta.-galactosidase pos., centrally nucleated fibers expressing human myosin heavy chains. Fibers originating from converted fibroblasts were indistinguishable from those obtained by injection of control cultures of lacZ-transduced satellite cells. MyoD-converted murine fibroblasts participated to muscle regeneration also in immunocompetent, syngeneic mice. Although antibodies from these mice bound to adenoviral infected cells in vitro, no inflammatory infiltrate was present in the graft site throughout the 3-wk study period. These data support the feasibility of an alternative approach to gene therapy of primary myopathies, based on implantation of large ***nos*** of genetically modified primary fibroblasts massively converted to myogenesis by adenoviral delivery of MyoD ex vivo.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:507817 CAPLUS <<LOGINID:20070126>>
DN 129:226294
TI Intermittent, repetitive corticosteroid-induced upregulation of platelet levels after adenovirus-mediated transfer to the liver of a chimeric glucocorticoid-responsive promoter controlling the thrombopoietin cDNA
AU Narumi, Ko; Suzuki, Motoyoshi; Song, Wenru; Moore, Malcolm A. S.; Crystal, Ronald G.
CS Division of Pulmonary and Critical Care Medicine, The New York Hospital-Cornell Medical Center, New York, NY, 10021, USA
SO Blood (1998), 92(3), 822-833
CODEN: BLOOAW; ISSN: 0006-4971
PB W. B. Saunders Co.
DT Journal
LA English
AB For many in vivo gene therapy clin. applications, it is desirable to control the expression of the transferred transgene using pharmacol. agents. To evaluate the feasibility of accomplishing this using corticosteroids, pharmacol. agents widely used in clin. medicine, we constructed replication deficient adenoviral (Ad) vectors contg. an expression cassette with a chimeric promoter comprised of five glucocorticoid response elements (GRE) and the chloramphenicol acetyltransferase reporter gene (AdGRE.CAT) or the murine thrombopoietin cDNA (AdGRE.mTPO). In vitro studies showed the vectors functioned as expected, with marked glucocorticoid-induced upregulation of the CAT or mTPO transgenes. To evaluate the inducibility of the GRE promoter in vivo, the AdGRE.CAT vector was administered i.v. to C57B1/6 mice, and CAT activity was quantified in liver before and after i.p. administration of dexamethasone. The GRE promoter activity was dependent on the dexamethasone dose, with a 100-fold increase in CAT expression with 50 .mu.g dexamethasone, similar to the levels obsd. in vivo with the Rous sarcoma virus long terminal repeat constitutive promoter. After dexamethasone administration, max. CAT activity was obsd. at day 2, with a slow decline to baseline levels by 2 wk. Based on these observations, we hypothesized that a single administration of an Ad vector-mediated transfer of the chimeric GRE inducible promoter driving the mTPO cDNA would enable repetitive administration of corticosteroids to repetitively upregulate platelet levels for 1 to 2 wk. The data show that this occurs, with dexamethasone administration every 3 wk assoc. with 1-wk elevations (at each 3-wk interval) of serum mTPO levels, megakaryocyte ***nos*** in ***bone*** ***marrow***, and platelet levels fourfold to sixfold over baseline. Thus, with the appropriate promoter, it is possible to use a commonly used pharmacol. agent to upregulate the expression of a newly transferred gene on demand.

RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:56402 CAPLUS <<LOGINID::20070126>>
DN 128:153017

TI Adenovector-mediated expression of human thrombopoietin cDNA in immune-compromised mice: insights into the pathophysiology of osteomyelofibrosis

AU Frey, Beat M.; Rafii, Shahin; Tetersen, Michael; Eaton, Dan; Crystal, Ronald G.; Moore, Malcolm A. S.

CS James Ewing Laboratory of Developmental Hematopoiesis, Sloan-Kettering Institute for Cancer Research, New York Hospital-Cornell Medical Center, New York, NY, 10021, USA

SO Journal of Immunology (1998), 160(2), 691-699
CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Thrombopoietin (TPO) cDNA can be effectively delivered in vivo by adenovectors. Immune normal mice (BALB/c) and syngeneic mice with variable degrees of immune dysfunction nu, SCID, and NOD-SCID were treated with an ***adenovirus*** **vector*** expressing the human TPO cDNA (AdTPO). Platelet peaks were higher in SCID and NOD-SCID mice compared with BALB/c and nu mice. Human plasma TPO concn. correlated with

the platelet counts. SCID and NOD-SCID mice exhibited also granulocytosis and increased ***nos***. of hemopoietic progenitors in ***bone*** **marrow***. Following platelet peak, BALB/c mice developed autoantibodies against murine TPO leading to thrombocytopenia and depletion of megakaryocytes and hemopoietic progenitors in ***bone*** **marrow***. AdTPO-treated SCID mice developed osteomyelofibrosis and extramedullary/extrasplenic hemopoiesis. In contrast, NOD-SCID mice with a similar magnitude of TPO overexpression did not show fibrotic changes in ***bone*** **marrow***. Thus, (1) a chronic high level of TPO overexpression stimulates megakaryocytopoiesis and myelopoiesis leading to thrombocytosis and granulocytosis; (2) increased megakaryocytopoiesis is not sufficient for development of secondary osteomyelofibrosis; the functionally deficient monocytes and macrophages of NOD-SCID mice probably prevented fibrotic marrow changes; (3) immune deficiency enhances expression of adenovirally mediated transgenes; and (4) xenogeneic transgene delivered by adenovector to a host with normal immune functions may induce loss of immune tolerance and autoimmune phenomenon.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 44 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:264084 CAPLUS <<LOGINID::20070126>>
DN 129:1014

TI Major effects of TPO delivered by a single injection of a recombinant adenovirus on prevention of septicemia and anemia associated with myelosuppression in mice: risk of sustained expression inducing myelofibrosis due to immunosuppression

AU Abina, M. A.; Tulliez, M.; Lacout, C.; Debili, N.; Villeval, J.-L.;

Pflumio, F.; Wendling, F.; Vainchenker, W.; Haddada, H.

CS INSERM U 362, Institut Gustave Roussy, Villejuif, 94805, Fr.

SO Gene Therapy (1998), 5(4), 497-506

CODEN: GETHEC; ISSN: 0969-7128

PB Stockton Press

DT Journal

LA English

AB Adenoviral vectors may be useful tools to deliver a cytokine in vivo. A single i.v. injection of an ***adenovirus*** **vector*** contg. the human thrombopoietin (TPO) cDNA (AdRSVhu TPO) was able to induce a thrombocytosis for more than 6 wk in SCID mice, assocd. with a megakaryocyte (MK) hyperplasia in different organs. A marrow and spleen fibrosis was obsd. at 6 wk. In immunocompetent mice, a single AdRSVhu TPO injection led to a moderate and transient thrombocytosis without myelofibrosis. To evaluate the usefulness of TPO for the prevention of secondary side-effects during an aplastic period, mice were subjected to a myeloablative regimen 7 days after the i.v. AdRSVhu TPO injection. In this setting, TPO prevented mortality by accelerating hematol. recovery. Survival was essentially related to an improvement in the leukopenia since all control mice died from septicemia. However, the effects of TPO may be potentiated by the release of inflammatory cytokines following the adenovirus infection: AdRSV.beta.galactosidase injected-mice had higher ***nos***. of BFU-E and CFU-GM in the marrow than PBS-injected mice. Myelosuppression induced transient immunosuppression responsible for a sustained expression and elevation of platelet ***nos***. for at least 5 mo. These results further suggest that TPO may be an effective therapy in diminishing hematol. complications related to myeloablative regimens, but emphasize that immunosuppression secondary to myelosuppression may lead to sustained expression assocd. with a risk of thrombosis and myelofibrosis when delivered by adenovirus vectors.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:257268 CAPLUS <<LOGINID::20070126>>
DN 133:171697

TI Enhancement of adenovirus-mediated gene transfer to human ***bone*** **marrow*** cells

AU Watanabe, Tsutomu; Kelsey, Linda; Ageitos, Ana; Kuszynski, Charles; Ino,

Kazuhiko; Heimann, Dean G.; Varney, Michelle T.; Shepard, H. Michael; Vaillancourt, Mel T.; Maneval, Daniel C.; Talmadge, James E.

CS Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha, NE, USA

SO Leukemia & Lymphoma (1998), 29(5/6), 439-451

CODEN: LELYEA; ISSN: 1042-8194

PB Harwood Academic Publishers

DT Journal

LA English

AB Adenovirus infection of CD34+ hematopoietic stem/progenitor cells is dependent on the multiplicity of infection (MOI), time of incubation, the vol. in which the co-incubation occurs, and the presence or absence of growth factors. Studies revealed that a brief co-incubation (1-8 h), resulted in low levels of transgene expression, suggesting that adenovirus infection of CD34+ cells occurs slowly, and optimal transduction requires a 24 h exposure to adenovirus. Infection by Ad/beta.-gal or Ad/p53 at a MOI of 500: 1 provided a high transduction efficiency but inhibited hematopoietic function. However, treatment at a MOI of 50-100 resulted in efficient transduction (10.7-15.7% pos.) without detectable toxicity. Secondary proof of adenovirus transgene expression was demonstrated by detection of mRNA for p53 in Ad/p53 infected stem cells. The authors conclude that a 24 h exposure to recombinant adenovirus encoding p53 or beta.-gal, at a MOI of 50-100 is optimal for in vitro gene transfer to BM cells and has no effect on hematopoietic function. Adenovirus-mediated transduction of BM cells can also be modulated by growth factors (IL-3, ***GM*** - ***CSF***, and G-CSF) with improved gene delivery and maintenance of hematopoietic function. In summary, adenovirus vectors can be used to transiently transduce stem cells, and conditions were defined to maximize expression and limit inhibitory effects on CD34+ cells. These data support continued investigation of this vector for local cytokine delivery and purging of stem cell products.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 46 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:234596 CAPLUS <<LOGINID::20070126>>
DN 126:316136

TI Intramarrow cytokine gene transfer by adenoviral vectors in dogs

AU Foley, R.; Ellis, R.; Walker, I.; Wan, Y.; Carter, R.; Boyle, M.; Braciak, T.; Addison, C.; Graham, Frank; Gauldie, Jack

CS Depts. Pathology Biology Medicine, McMaster Univ., Hamilton, ON, L8N 3Z5, Can.

SO Human Gene Therapy (1997), 8(5), 545-553

CODEN: HGTHE3; ISSN: 1043-0342

PB Liebert

DT Journal

LA English

AB Daily systemic administration of hematopoietic growth factors can be assocd. with dose-limiting systemic side effects. To overcome this, we have investigated hematopoietic cytokine gene transfer to the marrow cavity of dogs by direct intramarrow injection of adenoviral vectors. In marrow culture, replication-deficient (E1-deleted) adenoviral vectors were able to transduce marrow stromal cells, demonstrating 30-fold greater expression than from other marrow cell types. High-level (ng/mL) cytokine prodn. from transduced stromal cells persisted for 14 days in culture. Because adenovectors could efficiently transduce marrow stromal cells in culture, we investigated if stromal cells could also be transduced in vivo following direct intramarrow vector injection. Adenovectors with genes for interleukin 6 (IL-6) and Lac Z (beta.-galactosidase) were injected directly into the marrow cavity of dogs resulting in protein expression localized to within the treated marrow. To evaluate this approach further in dogs, we constructed a vector expressing biol. active canine granulocyte-macrophage colony stimulating factor (***GM*** - ***CSF***). 293 Cells infected with ADGM-CSF demonstrated prevalent ***GM*** - ***CSF*** mRNA by Northern blot and 135 +/- 30 ng/mL of protein as measured by ELISA. In vitro bioactivity of protein expressed was confirmed by canine GM colony-forming assay (CFU-GM). In vivo high-level protein prodn. was noted in supernatants of marrow aspirates 72 h following direct intramarrow administration of ADGM-CSF (baseline, 27 +/- 22 ng/mL, 72-h sample 921 +/- 461 ng/mL). A localized myeloid expansion of marrow and significant peripheral leukocytosis (neutrophilia) were noted in all ADGM-CSF-treated dogs. Peripheral blood changes lasted for up to 3 wk in dogs following single intramarrow injection. Thus, adenoviral cytokine expression from the marrow of a single large bone (ilium) led to compartmentalized expression of growth factor and an increase of hematopoiesis sufficient to cause peripheral growth changes in large animal model.

L5 ANSWER 47 OF 50 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 1998:108072 BIOSIS <<LOGINID::20070126>>
DN PREV199800108072

TI Lympholactin gene-modified ***bone*** **marrow*** dendritic cells act as more potent adjuvant for peptide delivery to induce antitumor immunity.

AU Cao, Xuetao [Reprint author]; Zhang, Weiping [Reprint author]; He, Long [Reprint author]; Yuan, Zhenglong [Reprint author]; Xie, Zhifang [Reprint author]; Ma, Shihua; Hamada, Hirofumi; Wang, Jianli [Reprint author]

CS Dep. Immunol., Second Military Medical Univ., 800 Xiang Yin Road, Shanghai 200433, China

SO Cancer Gene Therapy, (Nov.-Dec., 1997) Vol. 4, No. 6 CONF. SUPPL., pp.

S57. print.
Meeting Info.: Sixth International Conference on Gene Therapy of Cancer.
San Diego, California, USA. November 20-22, 1997.
ISSN: 0929-1903.

DT Conference: (Meeting)
Conference: Abstract; (Meeting Abstract)
Conference: (Meeting Poster)

LA English

ED Entered STN: 3 Mar 1998
Last Updated on STN: 3 Mar 1998

L5 ANSWER 48 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1996:590601 CAPLUS <<LOGINID::20070126>>
DN 125:214276

TI Methods of preparation and use of adenovirus vectors carrying therapeutic
genes and their therapeutic uses

IN Seth, Prem K.; Cowan, Kenneth

PA The Government of the United States of America, Re, USA

SO PCT Int. Appl., 145 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9625507	A2	19960822	WO 1996-US2336	19960216
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WO 9625507	A3	19961107		
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W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR

AU 9652974 A 19960904 AU 1996-52974 19960216

PRAI US 1995-390604 A2 19950217

WO 1996-US2336 W 19960216

AB Novel methods of constructing recombinant adenoviral vectors capable of
expressing human cDNAs, such as wild-type p53, WAF 1/Cip1/p21, p27/kip1, E.
coli cytosine deaminase, wild-type p16, TAM 67 (a jun/fos dominant neg.
mutant) and B7-1 and B7-2 are described. The method uses an adaptation of
the Clal method for prep. encapsidation-incompetent virus. A virus
carrying a second Clal site that is useful in the excision of the
5'-region of the viral genome is constructed for use in the method. The
invention further provides methods of inhibiting the proliferation of
cells, inhibiting the cell cycle of proliferating cells, and methods for
the eradication of cells, esp. cancer and diseased cells, by infecting the
cells with a recombinant ***adenovirus*** ***vector*** capable of
expressing human cDNAs. Comps. and methods of the invention are suitable
for treatment of a subject afflicted with a tumor wherein the cells of the
tumor, for example, lack the wild-type p53 allele and/or process a mutated
p53 gene. The invention addnl. provides a method for the use of
adenoviral vectors in the treatment of cancer cells, such as lung cancer
and breast cancer cells. The invention further provides methods for the
use of adenoviral vectors in cancer gene therapy as a mechanism for
purging ***bone*** ***marrow*** cells of contaminating tumor
cells, for eradicating cancer cells, and for preventing development of
cancer cells and tumors. The construction of an expression vector for the
expression of the wild-type p53 gene and its use to inhibit the
proliferation of breast cancer-derived cell lines is demonstrated.

L5 ANSWER 49 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1996:355136 CAPLUS <<LOGINID::20070126>>

DN 125:27195

TI Gene transfer into human ***bone*** ***marrow*** hematopoietic
cells mediated by adenovirus vectors

AU Watanabe, Tsutomu; Kuszynski, Charles; Ino, Kazuhiko; Heimann, Dean G.;
Shepard, H. Michael; Yasui, Yoshinori; Maneval, Daniel C.; Talmadge, James
E.

CS Department of Pathology/Microbiology and Internal Medicine, University of
Nebraska Medical Center, Omaha, NE, 68198-5660, USA

SO Blood (1996), 87(12), 5032-5039

CODEN: BLOOAW; ISSN: 0006-4971

PB Saunders

DT Journal

LA English

AB Human ***bone*** ***marrow*** mononuclear cells (BMMNCs) and
enriched CD34 pos. (CD34+) cells were transduced with adenovirus vectors
encoding Escherichia coli .beta.-galactosidase gene. Transductions were
carried out by 24-h incubation with adenovirus vectors at different
multiplicities of infections (moi). Efficacy of gene transfer into BM
cells and expression of the gene product (ie, .beta.-galactosidase) were
studied using X-Gal histochem. staining and flow cytometric anal. X-Gal
staining demonstrated that the percentage of pos. cells at moi of 5 to
500 was 3.4% to 34.5% for BMMNCs and 6.0% to 20.0% for enriched CD34+
cells. Similar results (1.5% to 35.7% for BMMNCs and 5.4% to 24.2% for
enriched CD34+ cells) were obtained with flow cytometric anal. using
fluorescein di-.beta.-D-galactopyranoside (FDG). Multicolor flow
cytometry anal., which included FDG, demonstrated that BM progenitors
(CD34+ or Cd34+CD38-), T cells (CD2+), B cells (CD19+), natural killer
cells (CD56+), granulocytes, and monocytes all expressed the adenovirus
transgene. To ascertain the effects of adenovirus vectors on normal BM
progenitors, the ***nos*** of colony-forming unit-
granulocyte/macrophage (CFU-GM), burst-forming unit-erythrocyte (BFU-E),

and high-proliferative potential - colony-forming cells (HPP-CFC) after
24-h incubation with adenovirus vectors were detd. When BMMNCs or
enriched CD34+ cells were incubated with adenovirus vectors at moi of 5
and 50, no significant differences in the ***nos*** of CFU-GM, BFU-E,
and HPP-CFC were obsd. in the ***nos*** of CFU-GM, BFU-E, and HPP-
CFC

were obsd. compared with the uninfected control cells. However, the
nos of CFU-GM were significantly (P < .01) decreased when BMMNCs
or enriched CD34+ cells were incubated with adenovirus vectors at a moi of
500, compared with the uninfected control cells. The adenovirus infected
cells, purified by cell sorting for FDG expression, were capable of
growing in culture and gave rise to various colonies (ie, CFI-GM, BFU-E,
and HPP-CFC). These data indicate that recombination adenovirus vectors
can be used to transfer genes to human BM hematopoietic cells with
expression of the exogenous gene at a high transduction efficiency.

L5 ANSWER 50 OF 50 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
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AN 94177638 EMBASE <<LOGINID::20070126>>

DN 1994177638

TI Hematopoietic supportive function of human ***bone*** ***marrow***
stromal cell lines established by a recombinant SV40- ***adenovirus***
vector

AU Aizawa S.; Yaguchi M.; Nakano M.; Toyama K.; Inokuchi S.; Imai T.; Yasuda
M.; Nabeshima R.; Handa H.

CS First Department Internal Medicine, Tokyo Medical College, 6-7-1
Nishi-shinjuku, Shinjuku-ku, Tokyo 160, Japan

SO Experimental Hematology, (1994) Vol. 22, No. 6, pp. 482-487.

ISSN: 0301-472X CODEN: EXHEBH

CY United States

DT Journal; Article

FS 025 Hematology

LA English

SL English

ED Entered STN: 6 Jul 1994

Last Updated on STN: 6 Jul 1994

AB We have previously reported the establishment of a variety of human
bone ***marrow*** stromal cell lines using a recombinant SV40-
adenovirus ***vector***. Using this vector, we obtained more
clonal stromal cells. Here, we have characterized these cells and
analyzed their capacity to support the proliferation and differentiation
of hematopoietic cells. The stromal cells were cocultured with
nonadherent human ***bone*** ***marrow*** cells used as
hematopoietic cells. The total numbers of hematopoietic cells and CFU-GM
in culture were counted every week. Two of the six stromal cell lines,
AA101 and HAS303, supported the proliferation and differentiation of
hematopoietic cells and CFU-GM for more than 9 weeks. Further,
granulocytes, macrophages, and megakaryocytes were detected when
cocultured with these cells. When hematopoietic cells were cocultured but
separated from the two stromal cell lines by a 0.45-.mu.m millipore
membrane to prevent their attachment, almost all CFU-GM disappeared within
7 weeks. The supportive stromal cells produced ***GM*** - ***CSF***
and IL-6. However, other cell lines producing these humoral factors did
not support hematopoietic cell proliferation for such a long time. These
findings suggest that these established human ***bone***
marrow stromal cell lines will be useful, in that analysis of
their supportive function in hematopoietic cell proliferation and
differentiation through cell-to-cell interaction will shed some light on
this area.

=> FIL STNGUIDE

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ENTRY	SESSION	
FULL ESTIMATED COST	189.93	192.03

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TOTAL

ENTRY	SESSION
CA SUBSCRIBER PRICE	-22.62 -22.62

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LAST RELOADED: Jan 19, 2007 (20070119/UP).

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ENTRY	SESSION	
FULL ESTIMATED COST	1.86	193.89

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TOTAL

ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00 -22.62

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=> s vector (7a) (HIF or endothelial PAS domain protein 1 or EPAS1 or MCP 1 or
GM CSF or PR39 or FGF or NOS)
L6 951 VECTOR (7A) (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR
EPAS1
OR MCP 1 OR GM CSF OR PR39 OR FGF OR NOS)

=> s l1 and l6
L7 39 L1 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 26 DUP REM L7 (13 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 26 ANSWERS - CONTINUE? Y/(N)/y

L8 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2006:1279866 CAPLUS <<LOGINID::20070126>>
DN 146:21264
TI Transducing cells with a retroviral vector associated with microbubbles
and administration of ultrasound
IN Porter, Colin David; Bamber, Jeffrey Colin; Taylor, Sarah Louise
PA The Institute of Cancer Research Royal Cancer Hospital, UK
SO PCT Int. Appl., 78pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006129080	A1	20061207	WO 2006-GB1972	20060531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2005-685384P P 20050531

US 2005-752020P P 20051221

AB Cell transduction providing targeted gene delivery is achieved using a retroviral vector assoc. with microbubbles and ultrasound exposure. Specifically, cationic lipid-shelled, perfluorocarbon gas-filled microbubbles and non-infectious murine leukemia virus lacking envelope protein are demonstrated to transduce TE671 human rhabdomyosarcoma cells when exposed to >0.4 MPa ultrasound. When microbubbles were mixed with virus particles immediately before addn. to cells, an approx.140-fold enhancement of transduction was obsd. over non-microbubble control groups, and a further 17-fold enhancement was obtained by binding the viral particles to the microbubble surface before transduction. Gene delivery followed ultrasound exposure for only 5 s, in contrast to 40 min required for a virus/liposome complex. The novel approach of using a phys. cell entry-based technique in combination with retroviral gene delivery has the effect of providing means for targeted, efficient, and/or stable gene delivery and assoc. expression of a transgene suitable for use in therapeutic applications. Ultrasound-dependent cell transduction allows spatial and temporal control over gene delivery and maximizes bioavailability of retrovirus.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1
AN 2006473741 EMBASE <<LOGINID::20070126>>
TI Efficient transient expression of human GM-CSF protein in Nicotiana benthamiana using potato virus X vector.
AU Zhou F.; Wang M.-L.; Albert H.H.; Moore P.H.; Zhu Y.J.
CS Y.J. Zhu, Hawaii Agriculture Research Center, 99-193 Aiea Heights Drive, Aiea, HI 96701, United States. jzhu@harc-hspa.com
SO Applied Microbiology and Biotechnology, (2006) Vol. 72, No. 4, pp. 756-762.
Refs: 36
ISSN: 0175-7598 CODEN: AMBIDG

CY Germany
DT Journal; Article
FS 004 Microbiology
022 Human Genetics
030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 16 Oct 2006

Last Updated on STN: 16 Oct 2006

AB The human granulocyte macrophage colony-stimulating factor (GM-CSF) is a glycoprotein with important clinical applications for the treatment of neutropenia and aplastic anemia and reducing infections associated with ***bone*** ***marrow*** transplants. We evaluated the potential for using a potato virus X (PVX) viral vector system for efficient expression of the biologically functional GM-CSF protein in Nicotiana benthamiana leaves. The ***GM*** - ***CSF*** gene was cloned into PVX viral expression ***vector***, driven with the CaMV 35S promoter. Gene transfer was accomplished by inoculating N. benthamiana leaves with the plasmid DNA of PVX ***vector*** containing the ***GM*** - ***CSF*** gene. The expression level of the recombinant GM-CSF protein was determined with ELISA and its size was confirmed by Western blot analysis. The results showed that: (1) leaf age significantly affects GM-CSF protein concentration with younger leaves accumulating 19.8 mg g (-1) soluble protein which is 2.6 times the concentration in older leaves, (2) recombinant protein accumulation within a given leaf declined slightly over time but was not significantly different between 7 and 11 days post-inoculation (dpi), and (3) the two leaves immediately above the inoculated leaves play an important role for GM-CSF accumulation in the younger leaves. Protein extracts of infected N. benthamiana leaves contained recombinant human GM-CSF protein in concentrations of up to 2% of total soluble protein, but only when the pair of leaves immediately above the inoculated leaves remained intact. The recombinant protein actively stimulated the growth of human TF-1 cells suggesting that the recombinant human ***GM*** - ***CSF*** expressed via PVX viral ***vector*** was biologically active. .COPYRGT. 2006 Springer-Verlag.

L8 ANSWER 3 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 2

AN 2006188818 EMBASE <<LOGINID::20070126>>

TI Manipulation of dendritic cells for host defence against intracellular infections.

AU McCormick S.; Santosuosso M.; Zhang X.Z.; Xing Z.

CS Z. Xing, Department of Pathology and Molecular Medicine, Centre for Gene Therapeutics, McMaster University, Hamilton, Ont. L8N 3Z5, Canada. xingz@mcmaster.ca

SO Biochemical Society Transactions, (2006) Vol. 34, No. 2, pp. 283-286. Refs: 18

ISSN: 0300-5127 CODEN: BCSTB5

CY United Kingdom

DT Journal; Conference Article

FS 004 Microbiology

015 Chest Diseases, Thoracic Surgery and Tuberculosis

026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 10 May 2006

Last Updated on STN: 10 May 2006

AB Dendritic cells (DCs) are an important innate immune cell type which is the bridge between innate and adaptive immunity. Mounting experimental evidence suggests that manipulating DCs represents a powerful means to enhance host defence against intracellular infectious diseases. We have developed several strategies to manipulate DCs either in vivo or in vitro for the purpose of enhancing the effect of vaccination or immunotherapeutics. In vivo delivery of transgene encoding GM-CSF (granulocyte/macrophage colony-stimulating factor), a DC-activating cytokine, increases the number and activation status of DCs at various tissue sites and enhances antimicrobial immune responses in murine models. Co-expression or co-delivery of ***GM*** - ***CSF*** gene transfer ***vector*** with an antimicrobial vaccine enhances microbial antigen-specific T-cell responses and immune protection. Murine ***bone*** ***marrow*** -derived DCs are being manipulated in vitro and exploited as a vaccine delivery system. Transduction of DCs with a virus-vectored tuberculosis vaccine is a powerful way to activate T-cells in vivo. Such genetically modified DC vaccines can be administered either parenterally or mucosally via the respiratory tract. .COPYRGT.2006 Biochemical Society.

L8 ANSWER 4 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2006397794 EMBASE <<LOGINID::20070126>>

TI Effects of fibroblast growth factor 18 on synthesis of alkaline phosphatase in ***bone*** ***marrow*** stem cells of rabbits cultured in vitro.

AU Tian J.; Yang F.; Li X.-Y.; Li L.; Xiang L.-B.; Zu Q.-M.; Fan Q.-Y.

CS J. Tian, Department of Orthopedics, General Hospital of Shenyang Military Area Command of Chinese PLA, Shenyang 110016 Liaoning Province, China

SO Chinese Journal of Clinical Rehabilitation, (10 Jun 2006) Vol. 10, No. 21, pp. 7-9.

Refs: 7

ISSN: 1671-5926 CODEN: ZLKHAH

CY China

DT Journal; Article

FS 029 Clinical Biochemistry

033 Orthopedic Surgery

LA Chinese

SL English: Chinese
ED Entered STN: 14 Sep 2006
Last Updated on STN: 14 Sep 2006

AB Aim: To construct stable eukaryotic expression ***vector*** of fibroblast growth factor (***FGF***) 18 and observe the effects of FGF-18 on synthesis of alkaline phosphatase in ***bone***
marrow stem cells (BMSCs) of rabbits cultured in vitro. Methods: The experiment was performed in the Orthopedics Oncology Institute of Chinese PLA and Dental Hospital, Fourth Military Medical University of Chinese PLA from October 2002 to March 2004. 1 Expression vector of pGEM-T-FGF18-3 and pSecTag2H were reconstructed into pSecTag2B-FGF18 plasmid with Kpn I and Not I enzyme; Protein of FGF-18 in cellular supernatant of transfected COS-7 was detected with ELISA, those above 2.1 times of A value in negative control were positive results. 2 Cellular supernatant was used to stimulate BMSCs. Cellular supernatant of transfected COS-7 were divided into 1:2 diluting group, 1:4 diluting group, 1:8 diluting group, 1:16 diluting group, 1:32 diluting group according to different proportions of DMEM containing calf serum (CS); Control group: Cellular supernatant of untransfected COS-7 was diluted with DMEM culture fluid, in which the volume fraction of CS was 0.02, according to 1:2.3 Synthesis of alkaline phosphatase in cells was inspected with enzyme kinetic method. Results: 1 Eukaryotic expression vector pSecTag2B-FGF18 was constructed successfully. 2 Stable expression of FGF-18 in transfected mammalian cells of COS-7 was inspected with ELISA method. A value of stock solution and cellular supernatant with the dilution of 1:10 were 2.1 times than that in negative control (P < 0.01). 3 72 hours after the stimulation of BMSCs with supernatant, A values of BMSC in 1:4 diluting group, 1:8 diluting group, 1:16 diluting group, 1:32 diluting group were obviously increased than that of control group (P < 0.01), which proved that there was promotion of FGF-18 on the synthesis of alkaline phosphatase in BMSCs of rabbits cultured in vitro. Conclusion: FGF-18 can remarkably promote synthesis of alkaline phosphatase in BMSCs of rabbits cultured in vitro, which suggests that FGF-18 plays a significant role in the differentiation of BMSCs and phenotypic maintenance of bone formation.

L8 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1130773 CAPLUS <<LOGINID::20070126>>

DN 143:400810

TI ***Bone*** ***marrow*** -relevant cells transfected with viral vector carrying genes involved in regulation of cell differentiation/proliferation and its uses in maintenance and/or repair of tissue

IN Hayashi, Shuji; Inoue, Makoto; Hasegawa, Mamoru

PA Dnavec Research Inc., Japan

SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005097988	A1	20051020	WO 2005-JP5144	20050322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI JP 2004-84992 A 20040323

AB A transformed ***bone*** ***marrow*** -relevant cell transfected with a viral vector carrying genes involved in regulation of cell differentiation/proliferation and its uses in maintenance and/or repair of tissue are provided. A method of diagnosing and treating a tissue suffering from a disease with the uses of the transformed ***bone*** ***marrow*** -relevant cell from mammal is also provided. The genes having the regulatory activity of cell differentiation/proliferation are selected from HGF, FGF, VEGF, PDGF, interleukin, GCSF, MCSF, SCF, IFN, Crx and Otx2 gene. The transformed ***bone*** ***marrow*** -relevant cell is useful in treating liver disease such as hepatitis, hepatic insufficiency, liver cirrhosis, and liver carcinoma. The transformed ***bone*** ***marrow*** -relevant cells decreased the liver enzyme (GOT, GPT and LDH) value in rat model with acute liver failure to the normal level.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:158813 CAPLUS <<LOGINID::20070126>>

DN 142:233371

TI Viral vector system that detects and responds to pathophysiological stimulus, grafted transgenic vigilant stem cells containing same, and therapeutic uses

IN Phillips, Ian M.; Tang, Yao Liang

PA University of South Florida, USA

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005017164	A1	20050224	WO 2004-US26195	20040811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2535680	A1	20050224	CA 2004-2535680	20040811
EP 1654365	A1	20060510	EP 2004-780953	20040811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRAI US 2003-494184P	P	20030811		
US 2003-494185P	P	20030811		
US 2003-513067P	P	20031021		
US 2003-513657P	P	20031023		
WO 2004-US26195	W	20040811		

AB ***Bone*** ***marrow*** -derived mesenchymal stem cells were transduced with a stimulus-responsive rAAV vector system that detects and responds to hypoxia in cardiac tissue. The first rAAV vector in the system is the "sensor" vector, and contains a cardiac-specific promoter linked to a sequence encoding an oxygen-sensitive chimeric transactivator contg. a GAL4 DNA binding domain (DBD), an oxygen-dependent degrdn. domain

from HIF-1.alpha., and a NF-kappa.B p65 activation domain (AD). The second rAAV vector is the "effector" vector, and contains a cardioprotective gene, such as heme oxygenase-1 gene, linked to a GAL4 UAS. The first rAAV vector expresses the chimeric transactivator specifically in the heart, and in response to hypoxia, the transactivator binds to the GAL4 upstream activating sequence (UAS) in the second rAAV vector. Binding of the transactivator to the UAS results in the expression of the cardioprotective gene. The rAAV vectors can be used to treat cells in a no. of other disease states, including diabetes, cancer, stroke, and atherosclerosis. These approaches to stem cell-based gene therapy provide a novel strategy not only for treatment but for prevention of cell destruction.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 3

AN 2005209009 EMBASE <<LOGINID::20070126>>

TI Human somatic PTPN11 mutations induce hematopoietic-cell hypersensitivity to granulocyte-macrophage colony-stimulating factor.

AU Chan R.J.; Leedy M.B.; Munugalavada V.; Voorhorst C.S.; Li Y.; Yu M.; Kapur R.

CS R.J. Chan, Herman B. Wells Ctr. Pediat. Res., 1044 W Walnut St, Indianapolis, IN 46202, United States. rchan@iupui.edu

SO Blood, (1 May 2005) Vol. 105, No. 9, pp. 3737-3742.

Refs: 39

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy
025 Hematology

LA English

SL English

ED Entered STN: 2 Jun 2005

Last Updated on STN: 2 Jun 2005

AB Juvenile myelomonocytic leukemia (JMML) is a lethal disease of young children characterized by hypersensitivity of hematopoietic progenitors to granulocyte-macrophage colony-stimulating factor (GM-CSF). Mutations in PTPN11, which encodes the protein tyrosine phosphatase Shp-2, are common in JMML. We hypothesized that PTPN11 mutations induce hypersensitivity of hematopoietic progenitors to GM-CSF and confer increased GM-CSF-stimulated phospho-extracellular signal-regulated kinase (Erk) levels. To test this hypothesis, the wild-type (WT) and 3 mutant Ptpn11 cDNAs (E76K, D61V, and D61Y) were transduced into murine ***bone*** ***marrow*** cells to examine GM-CSF-stimulated granulocyte-macrophage colony-forming unit (CFU-GM) growth, macrophage progenitor proliferation, and activation of the Ras signaling pathway. Expression of the Shp-2 mutants induced progenitor cell hypersensitivity to ***GM*** - ***CSF*** compared with cells transduced with ***vector*** alone or WT Shp-2. Macrophage progenitors expressing the Shp-2 mutants displayed both basal and ***GM*** - ***CSF*** -stimulated hyperproliferation compared with cells transduced with ***vector*** alone or WT Shp-2. Consistently, macrophage progenitors transduced with the Shp-2 mutants demonstrated constitutively elevated phospho-Erk levels and sustained activation of phospho-Erk following ***GM*** - ***CSF*** stimulation compared with ***vector*** alone or WT Shp-2. These data support the hypothesis that PTPN11 mutations induce hematopoietic progenitor hypersensitivity to GM-CSF due to hyperactivation of the Ras signaling axis and provide a

basis for the GM-CSF signaling pathway as a target for rational drug design in JMML. .COPYRG. 2005 by The American Society of Hematology.

L8 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:370529 CAPLUS <<LOGINID::20070126>>
DN 145:484184
TI Transfection of hypoxia-inducible factor 1.alpha. gene into human mesenchymal stem cells
AU Hu, Yuan; Yang, Liu; Duan, Xiaojun
CS Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China
SO Di-San Junyi Daxue Xuebao (2005), 27(9), 928-929
CODEN: DYXUE8; ISSN: 1000-5404
PB Di-San Junyi Daxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The HIF-1.alpha. gene was transfected into human mesenchymal stem cell (hMSCs) and the expression of HIF-1.alpha. gene was detd. The recombinant transcription virus ***vector*** of ***HIF*** -1.alpha. was constructed and expression of HIF-1.alpha. gene was detd. by RT-PCR. The expression of HIF-1.alpha. in hMSCs increased compared with normal hMSCs. HIF-1.alpha. gene was transfected into hMSCs successfully, which laid a foundation for bone tissue engineering.

L8 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:610402 CAPLUS <<LOGINID::20070126>>
DN 142:86546
TI Enhancer-deleted retroviral vectors restore high levels of superoxide generation in a mouse model of CGD
AU Schwickerath, Oliver; Brouns, Gaby; Thrasher, Adrian; Kinnon, Christine; Roes, Juergen; Casimir, Colin
CS Molecular Immunology Unit, Institute of Child Health, London, WC1E 6JJ, UK
SO Journal of Gene Medicine (2004), 6(6), 603-615
CODEN: JGMEFG; ISSN: 1099-498X
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB Background: Retroviral vectors possess many advantages for use in gene therapy protocols, esp. within the hematopoietic system. A no. of attendant problems, however, still limit their safety in clin. application. The effects of the enhancer present in the retroviral long terminal repeat (LTR) are a major concern for the clin. usage of such vectors, as they can exert a powerful regulatory influence on the genes that surround them. Methods: To improve the safety and widen the applicability of retroviral vectors for use in gene therapy we have developed an enhancer-deleted (.DELTA.-LTR) retroviral vector that retained high titer and demonstrated transcriptional activity in myeloid cells. Results: When used to correct a mouse model of autosomal recessive chronic granulomatous disease, the .DELTA.-LTR vectors gave acceptable levels of gene transfer to mouse ***bone*** ***marrow*** cells. Evidence for a slight preferential expression in myeloid cells was obtained with all the vectors studied. Nitroblue tetrazolium assay of superoxide generation in mouse ***bone*** ***marrow*** derived hematopoietic colonies revealed that transduction with .DELTA.-LTR vectors could restore functional NADPH oxidase to cells from these animals. Superoxide assay of peripheral blood confirmed that, although relatively low ***nos*** of cells were transduced, the .DELTA.-LTR ***vector*** was capable of reconstituting very high levels of oxidase activity, comparable to that obtained from normal cells. Conclusions: The .DELTA.-LTR vector described here could provide the basis for a new generation of retroviral vectors with improved safety.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:154455 CAPLUS <<LOGINID::20070126>>
DN 138:199989
TI Novel human .alpha.CP isoforms, binding of .alpha.CP and HuR, and uses thereof for modulating gene expression, stabilizing hypoxia regulated mRNAs (such as VEGF) and inducing angiogenesis
IN Guy, Louis-Georges
PA Angiogene Inc., Can.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2003016343 A2 20030227 WO 2002-CA1275 20020816
WO 2003016343 A3 20030925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, KZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002322911 A1 20030303 AU 2002-322911 20020816

US 2004241797 A1 20041202 US 2004-486865 20040213
PRAI US 2001-312397P P 20010816
WO 2002-CA1275 W 20020816

AB The present inventor has discovered novel human .alpha.CP isoforms, .alpha.CP1A, .alpha.CP1B, .alpha.CP2A, and .alpha.CP2B. The present inventor has also discovered that .alpha.CP polypeptides and HuR bind each other. The present inventor has further discovered that .alpha.CP polypeptides are capable of binding mRNAs mols., such as VEGF mRNA, for stabilizing the same. The present inventor has further discovered that HuR is capable of binding mRNA mols. previously unknown to be bound by HuR. The invention also describes mRNA stabilizing elements and consensus sequences involved in binding of .alpha.CP1, .alpha.CP2 and HuR proteins to mRNAs. In general, the invention features an isolated or purified nucleic acid mol. that encodes or corresponds to a human .alpha.CP. The present invention describes methods for modulating gene expression, stabilizing VEGF mRNAs, for inducing angiogenesis, for treating various mammalian diseases including coronary and cardiac diseases and for identifying modulators of gene expression by using human proteins called .alpha.CP1, .alpha.CP2 and HuR.

L8 ANSWER 11 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2003:451286 BIOSIS <<LOGINID::20070126>>
DN PREV200300451286
TI Enhancement of dendritic cell vaccine by improving in vivo antigen presentation through lentiviral ***vector*** modified murine ***bone*** ***marrow*** cells and ***GM*** - ***CSF*** stimulation.
AU Wiegand, Jessica [Reprint Author]; Cui, Yan [Reprint Author]
CS Gene Therapy Program and Stanley S. Scott Cancer Center, Departments of Medicine and Genetics, Louisiana State University Health Sciences Center, New Orleans, LA, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 355-356. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research, Washington, DC, USA, July 11-14, 2003.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 Oct 2003
Last Updated on STN: 1 Oct 2003

L8 ANSWER 12 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2003:369038 BIOSIS <<LOGINID::20070126>>
DN PREV200300369038
TI High Level Expression of the Cancer/Testis Antigen NY-ESO-1 and Human ***GM*** - ***CSF*** in Dendritic Cells with a Bicistronic Retroviral ***Vector***
AU Balchu, Ramesh B. [Reprint Author]; Moreno, Amberly M.; Szmania, Susann; Gupta, Sushil K.; Zhan, Fenguan; Rosen, Nancy; Spagnoli, Giulio C.; Shaughnessy, John; Barlogie, Bart; Tricot, Guido J.; van Rhee, Frits
CS Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR, USA
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 5554. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology, Philadelphia, PA, USA, December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

AB Multiple myeloma (MM) is an incurable disease characterized by the uncontrolled expansion of malignant plasma cells predominantly in ***bone*** ***marrow***. Tumor specific genes delivered to dendritic cells (DC) have been used for the generation of cytotoxic T cells (CTL) to kill myeloma cells, but their application has been limited on the one hand by low viral titers resulting in low transduction efficiency and poor protein production, and on the other hand by immunogenicity of the selectable marker and poor viability of the DC. We addressed these limitations by creating a multi-purpose master vector (pMV) for immunotherapy and cloned NY-ESO-1 cancer/testis gene, which is highly expressed in approx 50% of advanced myeloma patients. pMV was constructed from a Mo-MuLV based retroviral backbone with the following features: 1) an extended packaging signal and a splice acceptor region to facilitate protein production, 2) a non-immunogenic selectable marker, dihydrofolate reductase-L22Y (DHFR^{L22Y}) to exclude the generation of CTLs against the selectable marker, 3) an internal ribosomal entry site (IRES) between the tumor specific gene (NY-ESO-1) and the selectable marker DHFR^{L22Y} for co-expression of two heterologous genes minimizing the possibility of differential expression of these two genes, 4) hGM-CSF driven by the HTLV promoter to enhance DC viability and augment the immune response. Recombinant pseudotyped virus of pMV-NY-ESO-1 was generated with vesicular stomatitis virus G envelope protein (VSV-G) for efficient transduction. Genomic integration of recombinant viral genome was established by genomic PCR amplification of transduced DC for Long terminal repeats (LTR) of the vector. RT-PCR analysis and Western blot

analysis confirmed NY-ESO-1 gene transcription and protein production. Immunofluorescence staining of the transduced DC showed a high level expression of GM-CSF protein with high transduction efficiency. DC phenotype is unaltered after transduction, selection with trimetrexate (TMTX) and approx 85% of DC express NY-ESO-1, and secrete approx 50 ng of GM-CSF per million cells.

L8 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:101291 CAPLUS <<LOGINID::20070126>>

DN 134:161880

TI cDNAs encoding the Flt-3 receptor ligand and their use as adjuvants in vector vaccines

IN Hermanson, Gary George

PA Vical Inc., USA

SO PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001009303	A2	20010208	WO 2000-US20679	20000731
WO 2001009303	A3	20010816		

W: CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAL US 1999-146170P P 19990730

AB A method of increasing the strength of the immune response of vector vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by administering in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

L8 ANSWER 14 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
DUPLICATE 4

AN 2001403731 EMBASE <<LOGINID::20070126>>

TI Replication-defective recombinant Semliki Forest virus encoding ***GM***
CSF as a ***vector*** system for rapid and facile generation of autologous human tumor cell vaccines.

AU Withoff S.; Glazenburg K.L.; Van Veen M.L.; Hospers G.A.P.; Storkel S.

CS Dr. K.L. Glazenburg, Department of Medical Microbiology, Molecular Virology Section, University of Groningen, Ant. Deusinglaan 1, 9713 AV Groningen, Netherlands

SO Gene Therapy, (2001) Vol. 8, No. 20, pp. 1515-1523.

Refs: 52

ISSN: 0969-7128 CODEN: GETHEC

CY United Kingdom

DT Journal; Article

FS 004 Microbiology

016 Cancer

030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 6 Dec 2001

Last Updated on STN: 6 Dec 2001

AB This paper describes the production of recombinant Semliki Forest virus encoding murine or human granulocyte - macrophage colony-stimulating factor (GM-CSF) and the capacity of these vectors to transduce murine and human tumor cells ex vivo. High-titer stocks (up to 3×10^9 particles/ml) of conditionally infective, replication-defective, recombinant SFV particles were generated using the SFV Helper-2 system. It is shown that the recombinant SFV/GM-CSF virus, as well as recombinant SFV carrying the β -galactosidase reporter gene, efficiently transduce both murine tumor cell lines as well as primary human renal carcinoma cells. Using ELISA's specific for GM-CSF, levels of GM-CSF production by the cells were determined. Levels of murine GM-CSF (mGM-CSF) produced by SFV/mGM-CSF transduced renal cell cancer cultures were equal to or higher than corresponding levels reported in the literature after transduction of similar renal carcinoma cell cultures using a retroviral vector system. The biological activity of GM-CSF was demonstrated by using cells which are dependent on GM-CSF for growth and by using primary ***bone*** ***marrow*** cells. All the transduced cell cultures (including the human renal cell carcinoma samples) produced GM-CSF for up to at least 4 days after transduction. The results imply that the recombinant SFV system can be used for rapid and facile preparation of autologous cancer cell vaccines.

L8 ANSWER 15 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2000112930 EMBASE <<LOGINID::20070126>>

TI Transgenic expression of granulocyte-macrophage colony-stimulating factor induces the differentiation and activation of a novel dendritic cell population in the lung.

AU Wang J.; Snider D.P.; Hewlett B.R.; Lukacs N.W.; Gauldie J.; Liang H.;

Xing Z.

CS Z. Xing, Health Sciences Centre, Dept. of Pathol. and Molec. Medicine, McMaster University, Hamilton, Ont. L8N 3Z5, Canada.
xingz@fhs.cmu.mcmaster.ca

SO Blood, (1 Apr 2000) Vol. 95, No. 7, pp. 2337-2345.

Refs: 46

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 13 Apr 2000

Last Updated on STN: 13 Apr 2000

AB The role of granulocyte-macrophage colony-stimulating factor (GM-CSF) in the differentiation of dendritic cells (DCs) during pulmonary viral infection was investigated by using a mouse model of ***GM***
CSF transgene expression established with an adenoviral ***vector*** (AdGM-CSF). GM-CSF gene transfer resulted in increased levels of GM-CSF in the lung, which peaked at day 4 and remained increased up to day 19. A striking cellular response composed predominantly of macrophage-like cells was observed in the lung receiving AdGM-CSF but not control vector. By FACS analysis, the majority of these cells were identified at an early time point as macrophages and later as mature/activated myeloid DCs characterized by CD11b(bright), CD11c(bright), MHC class II(bright), and B7.1(bright). In contrast, GM-CSF had a weak effect on a small DC population that was found present in normal lung and was characterized by CD11c(bright) and CD11b(low). By immunohistochemistry staining for MHC II, the majority of activated antigen-presenting cells were localized to the airway epithelium and peribronchial/perivascular areas in the lung. A concurrently enhanced Th1 immune response was observed under these conditions. The number of CD4 and CD8 T cells was markedly increased in the lung expressing GM-CSF, accompanied by increased release of interferon (IFN).gamma. in the lung. Furthermore, lymphocytes isolated from either lung parenchyma or local draining lymph nodes of these mice but not the control mice released large amounts of IFN.gamma. on adenoviral antigen stimulation in vitro. These findings reveal that GM-CSF promotes the differentiation and activation of a myeloid DC population primarily by acting on macrophages during pulmonary immune responses. (C) 2000 by The American Society of Hematology.

L8 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:536159 CAPLUS <<LOGINID::20070126>>

DN 133:220701

TI Enforced P-glycoprotein pump function in murine ***bone***

marrow cells results in expansion of side population stem cells in vitro and repopulating cells in vivo

AU Bunting, Kevin D.; Zhou, Sheng; Lu, Taihe; Sorrentino, Brian P.

CS Division of Experimental Hematology, Department of Hematology/Oncology, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA

SO Blood (2000), 96(3), 902-909

CODEN: BLOOAW; ISSN: 0006-4971

PB American Society of Hematology

DT Journal

LA English

AB The human multidrug resistance-1 (MDR1) gene product, P-glycoprotein (P-gp), is well known for its ability to confer drug resistance; however, recent evidence suggests that P-gp expression can have more general effects on cellular development. In support of this idea, it was previously shown that retroviral-mediated MDR1 expression in murine ***bone*** ***marrow*** cells resulted in the expansion of stem cells in culture and in the development of a myeloproliferative syndrome in transplanted mice. It is now reported that MDR1-mediated stem cell expansion is assocd. with an increase in side population (SP) stem cells, defined by Hoechst dye staining. Transduction of murine ***bone*** ***marrow*** cells with an MDR1 retroviral vector resulted in an almost 2 log increase in SP cell nos. over 12 days in culture, whereas there was a rapid loss of SP cells from control cultures. Stem cell amplification was not limited to ex vivo expansion cultures but was also evident when MDR1-transduced cells were directly transplanted into irradiated mice. In these cases, stem cell expansion was assocd. with relatively high ***vector*** copy ***nos*** in stem cell clones. As previously reported, some cases were assocd. with a characteristic myeloproliferative syndrome. A functionally inactive MDR1 mutant cDNA was used to show that P-gp pump function was required both for amplification of phenotypically defined SP cells and functionally defined repopulating cells. These studies further support the concept that ABC transporter function can have important effects on hematopoietic stem cell development.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2000131423 EMBASE <<LOGINID::20070126>>

TI Local and systemic effects after adenoviral transfer of the murine granulocyte-macrophage colony-stimulating factor gene into mice.

AU Burger J.A.; Baird S.M.; Powell H.C.; Sharma S.; Eling D.J.; Kipps T.J.

CS Dr. J.A. Burger, Department of Medicine, Division of Hematology/Oncology, University of California, 9500 Gilman Drive, San Diego, CA 92093-0663,

United States, j1burger@ucsd.edu
 SO British Journal of Haematology, (2000) Vol. 108, No. 3, pp. 641-652.
 Refs: 41
 ISSN: 0007-1048 CODEN: BJHEAL
 CY United Kingdom
 DT Journal; Article
 FS 022 Human Genetics
 025 Hematology
 037 Drug Literature Index
 LA English
 SL English
 ED Entered STN: 27 Apr 2000
 Last Updated on STN: 27 Apr 2000
 AB Vectors encoding immunostimulatory genes are under investigation for their use as adjuvants for immunotherapy. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a prominent candidate gene for this approach because this cytokine can prime immune responses to 'self' tumour or other weak antigens. Prior studies suggested that GM-CSF induces accumulation and differentiation of antigen-presenting cells, particularly dendritic cells that can initiate immunity. To evaluate this model in vivo, we performed i.m. and i.p. injections of an adenovirus ***vector*** encoding murine ***GM*** - ***CSF*** (Ad-mGM-CSF) and evaluated local and systemic effects. After intramuscular injection, local changes were characterized by the accumulation of myeloid cells, a subsequent infiltration of lymphocytes and then myonecrosis. Intraperitoneal injection also induced an accumulation of myeloid cells, an increase in CD3+ positive T and a decrease in B220-positive B lymphocytes. Expression of the dendritic cell marker CD11c on 48 +/- 9% of the peritoneal cells (n = 6) along with high levels of surface MHC class II, a characteristic morphology, and endocytosis of FITC-dextran suggested in vivo differentiation of dendritic cells after i.p. injection of Ad-mGM-CSF. Systemic effects were observed after i.m. and i.p. injection of Ad-mGM-CSF. All mice developed hepatosplenomegaly resulting from extramedullary haematopoiesis. These changes were specific to GM-CSF as they were not seen in mice injected with an adenovirus vector without a transgene. Our observations indicate that adenoviral transfer of GM-CSF is a powerful tool for inducing local and systemic expansion of haematopoietic cells. The local expansion of myeloid cells displaying signs of dendritic cell differentiation, as characterized for the peritoneal cell compartment, can explain the potency of GM-CSF when used as an adjuvant in genetic immunotherapy.

L8 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2001:109279 CAPLUS <<LOGINID:20070126>>
 DN 135:252485
 TI Expression of lipofect AMINE mediated human ***GM*** - ***CSF*** eukaryotic expressing ***vector*** in HFCL cells
 AU Ma, Lijun; Wang, Guanjin; Li, Liang; Feng, Kai; Bai, Cixian; Pei, Xuetao
 CS Department of Hematology & Oncology, The First Clinical College, Nornan Bethune University of Medical Sciences, Changchun, 130021, Peop. Rep. China
 SO Zhonghua Xueyexue Zazhi (2000), 21(12), 624-627
 CODEN: CHTCD7; ISSN: 0253-2727
 PB Zhongguo Yixue Kexueyuan Xueyexue Yanjiusuo
 DT Journal
 LA Chinese
 AB An eukaryotic expressing vector-pIRES1neo/hGM-CSF was constructed and expressed in human ***bone*** ***marrow*** stromal cell line HFCL. Human granulocyte/macrophage colony-stimulating factor cDNA was inserted into an effective eukaryotic expressing vector-pIRES1neo which contains the human cytomegalovirus (CMV) major immediate early promoter/enhancer and the internal ribosome entry site (IRES) of the encephalomyocarditis virus 9FCMV. HFCL cells were transfected with the recombinant vector pIRES1neo/hGM-CSF by liposome-mediated gene transfer method. Integration of hGM-CSF in the genome, transcription of its mRNA and expression of its protein in the transfected HFCL cells were assayed by Southern blot, Northern blot, ELISA and hGM-CSF dependent cell line TF-1. hGM-CSF cDNA was integrated into HFCL genome successfully, hGM-CSF mRNA was transcribed and hGM-CSF protein was expressed of ng/106 cells by ELISA and (6.56 +/- 0.16) x 103 U/106 cells per day by TF-1 cell assay in the supernatant. The recombinant vector proved to be stably expressed in HFCL cells and the bio. activity of hGM-CSF was detectable in the supernatant of the transfected cells.

L8 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2002:196091 CAPLUS <<LOGINID:20070126>>
 DN 137:74143
 TI MDR1 gene expression in NOD/SCID repopulating cells after retroviral gene transfer under clinically relevant conditions
 AU Schilz, A. J.; Schiedmeier, B.; Kuhlcke, K.; Fruehauf, S.; Lindemann, C.; Zeller, W. J.; Grez, M.; Fauser, A. A.; Baum, C.; Eckert, H.-G.
 CS EUFETS GmbH, Idar-Oberstein, 55743, Germany
 SO Molecular Therapy (2000), 2(6), 609-618
 CODEN: MTOHCK; ISSN: 1525-0016
 PB Academic Press
 DT Journal
 LA English
 AB We have adapted a recently published protocol for retroviral gene transfer into hematopoietic cells with respect to clin. requirements such as large-vol. ***vector*** stock generation, adequate cell source, high cell ***nos***, and serum-free conditions. We present data on transduction efficacy and expression of the multidrug resistance 1 (MDR1) gene in human CD34+ cells from mobilized peripheral blood (PB) mediated by

a gibbon ape leukemia virus (GALV)-pseudotyped retroviral vector. Using a 1-day cytokine-mediated prestimulation, consisting of human interleukin (IL)-3, IL-6, stem cell factor (SCF), Flt-3 ligand (FL), and thrombopoietin (TPO), followed by a 3-day transduction procedure, we were able to detect up to 51% CD34+ cells expressing MDR1. Xenotransplantation of transduced cells into NOD/LiSz-scid/scid (NOD/SCID) mice resulted in a mean engraftment level of 23% (0.1 to 87%). As shown by quant. PCR anal., a mean of 12.7% (range 0.3 to 55%) of the engrafted human cells in the ***bone*** ***marrow*** of chimeric mice contained the MDR1 cDNA. Furthermore, enhanced expression of MDR1 above control levels was detected in up to 15% of the engrafted human cell population. Our data suggest that NOD/SCID repopulating cells derived from mobilized PB can be transduced efficiently with existing retroviral vector systems under clin. applicable conditions. (c) 2000 Academic Press.

RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 AN 2001:311471 BIOSIS <<LOGINID:20070126>>
 DN PREV200100311471
 TI Enhanced hematopoietic recovery after coinfusion of hematopoietic stem cells and ***bone*** ***marrow*** stromal cells which were transfected with adenoviral ***vector*** carrying the ***GM*** - ***CSF*** gene in a mouse BMT model.
 AU Kim, Hyo Jung [Reprint author]; Kim, Sang-Hee [Reprint author]; Suh, Cheolwon [Reprint author]; Kim, Sung Bae [Reprint author]; Park, Jung Sun; Cho, Hwa Jeong; Lee, Jung Shin [Reprint author]; Kim, Woo Kun [Reprint author]
 CS Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
 SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2; pp. 387b, print.
 Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 27 Jun 2001
 Last Updated on STN: 19 Feb 2002
 AB The ***bone*** ***marrow*** mesenchymal stem cells are a heterogeneous population. The proliferation of hematopoietic stem cells and their differentiation occurs in association with stromal cells as well as the cytokines and extracellular matrix components produced by the stromal cells. The use of cultured stromal cells as a vehicle for cell or gene therapy is an attractive method for rapid engraftment after BMT. The aims of this study was to evaluate the effects of coinfused BM stromal cells which were transfected with adenoviral ***vector*** carrying the ***GM*** - ***CSF*** gene on hematopoietic engraftment in a mouse BMT model. C3H strain mice (male, 8 weeks old) were irradiated (8.5Gy) and infused with BM stem cells (5*105) via ophthalmic vein. MS-5 cells (mouse BM stromal cell line) were transfected with recombinant adenovirus carrying mouse GM-CSF (Adv-GMCSF, 50M.O.I) or E1 region deleted adenovirus (DELTA E1-Adv). Experiment was divided with 3 groups: coinfusion of A) BM stem cells + control MS-5 cells (5*106), B) BM stem cells + MS-5 cells transfected with DELTA E1-Adv and C) BM stem cells + MS-5 cells transfected with Adv-GMCSF. On day 14 after BMT, mice were sacrificed and their spleens were examined for CFU (colony forming units in spleen) assay. BM cells were obtained by flushing femurs and tibias, culture for CFU (colony forming units in culture) assay was done for 2 weeks. To confirm the engraftment of MS-5 cells in tissues, total cellular RNA was extracted from BM, spleen and liver for RT-PCR (adenovirus type 5 CMV region and GM-CSF). The number of mice were 3 at each study group. Transfection efficiency of Adv-GMCSF at 50 M.O.I on MS-5 was 60%. By RT-PCR, expected bands of the PCR product were observed in MS-5 cells-Adv-GMCSF, BM, spleen, liver extracts. The colony counts of CFU assay were significantly higher in group C (A : B : C = 5.8 : 1 : 18.5) in group C, the colony size is larger and fibroblast-like stromal cells were found under the colony formations. CFU showed increased and packed with primitive progenitor cells in group C. In this study we found that BM stromal cells are efficient vehicles for transfection of adenovirus carrying the GM-CSF gene and they have an ability to home into the ***bone*** ***marrow***. Coinfused MS-5 cells - Adv-GMCSF can accelerate the ability of the hematopoietic recovery in a mouse BMT model.

L8 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 1999:595358 CAPLUS <<LOGINID:20070126>>
 DN 131:223487
 TI Induction of apoptotic or cytotoxic gene expression by adenovirus-mediated gene delivery
 IN McDonnell, Timothy J.; Swisher, Stephen G.; Fang, Bingliang; Bruckheimer, Elizabeth M.; Sarkiss, Mona G.; Ji, Li; Roth, Jack A.
 PA Board of Regents, the University of Texas System, USA
 SO PCT Int. Appl., 151 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9946371 A2 19990916 WO 1999-US5359 19990311
 WO 9946371 A3 20000824
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2322663 A1 19990916 CA 1999-2322663 19990311
 AU 9931837 A 19990927 AU 1999-31837 19990311
 AU 762493 B2 20030626
 EP 1070122 A2 20010124 EP 1999-913854 19990311
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
 US 6899870 B1 20050531 US 1999-266465 19990311
 US 2006002895 A1 20060105 US 2005-141678 20050531
 PRAI US 1998-77541P A2 19980311
 US 1999-266465 A3 19990311
 WO 1999-US5359 W 19990311

AB The present invention relates to adenoviral vectors contg. propapoptotic genes of the Bcl-2 gene family and their use in cancer therapy. The vector may addnl. contain a second gene, e.g., one encoding a tumor suppressor, a cytokine, a receptor, a differentiating agent, or a nucleic acid antisense to an oncogene. Thus, adenoviral vector Ad-Bax, contg. a truncated Bax gene encoding a Bax protein contg. an intact BH3 death domain, induced apoptosis in human breast cancer cells.

L8 ANSWER 22 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 5

AN 2000018994 EMBASE <<LOGINID::20070126>>

TI Transduction of dendritic cell progenitors with a retroviral vector encoding viral interleukin-10 and enhanced green fluorescent protein allows purification of potentially tolerogenic antigen-presenting cells.

AU Takayama T.; Tahara H.; Thomson A.W.

CS A.W. Thomson, W1544 Biomedical Science Tower, Univ. of Pittsburgh Medical

Center, 200 Lothrop Street, Pittsburgh, PA 15213, United States.
 thomsonaw@msx.upmc.edu

SO Transplantation, (27 Dec 1999) Vol. 68, No. 12, pp. 1903-1909. Refs: 48

ISSN: 0041-1337 CODEN: TRPLAU

CY United States

DT Journal; Conference Article

FS 004 Microbiology

022 Human Genetics

026 Immunology, Serology and Transplantation

LA English

SL English

ED Entered STN: 20 Jan 2000

Last Updated on STN: 20 Jan 2000

AB Background. Dendritic cells (DC) are important antigen-presenting cells that play critical roles in the initiation and modulation of immune responses. Genetic engineering of DC to express immunosuppressive molecules is a novel approach to the inhibition of allograft rejection. Retroviral delivery of viral interleukin (vIL)-10 to replicating myeloid DC progenitors (DCp) impairs their T-cell stimulatory capacity and promotes the induction of antigen-specific T-cell hyporesponsiveness. However, transduction efficiency with retroviral vectors is comparatively low. Enhanced green fluorescent protein (EGFP) is important both as a marker of gene transduction and for the selection of transduced cells. Our aims were to construct a retroviral vector encoding both vIL-10 and EGFP, to positively select transduced DC, and to assess the impact of these highly purified, vIL-10-secreting antigen-presenting cells on allogeneic T-cell responses. Methods. DCp propagated from ***bone*** marrow of C57BL/10 (H2b) mice in granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***)+IL-4 were transduced with a retroviral ***vector*** encoding both vIL-10 and EGFP by centrifugal enhancement. Gene transfer efficiency was determined by flow cytometry. Transduced cells were flow sorted, and vIL-10 secretion was quantified by ELISA. DC function was assessed by the ability of the cells to induce naive allogeneic (C3H; H2(k)) T-cell proliferation and cytotoxic T lymphocyte generation. Results. Retrovirally transduced DC expressed both vIL-10 and EGFP gene products. Approximately 20% of unsorted cells expressed EGFP, as determined by flow cytometry. vIL-10 was produced at a mean rate of 31 ng/40 hr/106 cells. After sorting, the incidence of EGFP+ DC was increased dramatically to at least 95%, and the production of vIL-10 was increased approximately three- to fourfold, to a mean of 107 ng/40 hr/106 cells. These highly purified, vIL-10-secreting DC exhibited markedly diminished capacity to induce allogeneic T-cell proliferative and cytotoxic responses. Conclusions. DCp retrovirally transduced to express both vIL-10 and EGFP can be rapidly identified and sorted to high levels of purity. The availability of highly enriched preparations of vIL-10-transduced DC facilitates studies of their immunoregulatory function and may enhance their therapeutic potential in transplantation or autoimmune disease.

L8 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1996:590601 CAPLUS <<LOGINID::20070126>>

DN 125:214276

TI Methods of preparation and use of adenovirus vectors carrying therapeutic genes and their therapeutic uses

IN Seth, Prem K.; Cowan, Kenneth

PA The Government of the United States of America, Re, USA
 SO PCT Int. Appl., 145 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9625507	A2	19960822	WO 1996-US2336	19960216
WO 9625507	A3	19961107		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR				
AU 9652974	A	19960904	AU 1996-52974	19960216
PRAI US 1995-390604	A2	19950217		
WO 1996-US2336	W	19960216		

AB Novel methods of constructing recombinant adenoviral vectors capable of expressing human cDNAs, such as wild-type p53, WAF1/Cip1/p21, p27/kip1, E. coli cytosine deaminase, wild-type p16, TAM 67 (a jun/fos dominant neg. mutant) and B7-1 and B7-2 are described. The method uses an adaptation of the Clal method for prep. encapsidation-incompetent virus. A virus carrying a second Clal site that is useful in the excision of the 5'-region of the viral genome is constructed for use in the method. The invention further provides methods of inhibiting the proliferation of cells, inhibiting the cell cycle of proliferating cells, and methods for the eradication of cells, esp. cancer and diseased cells, by infecting the cells with a recombinant adenovirus vector capable of expressing human cDNAs. Comps. and methods of the invention are suitable for treatment of a subject afflicted with a tumor wherein the cells of the tumor, for example, lack the wild-type p53 allele and/or process a mutated p53 gene. The invention addnl. provides a method for the use of adenoviral vectors in the treatment of cancer cells, such as lung cancer and breast cancer cells. The invention further provides methods for the use of adenoviral vectors in cancer gene therapy as a mechanism for purging ***bone*** marrow cells of contaminating tumor cells, for eradicating cancer cells, and for preventing development of cancer cells and tumors. The construction of an expression vector for the expression of the wild-type p53 gene and its use to inhibit the proliferation of breast cancer-derived cell lines is demonstrated.

L8 ANSWER 24 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 1994:431620 BIOSIS <<LOGINID::20070126>>

DN PREV199497444620

TI Granulocyte-macrophage colony-stimulating factor expression is regulated at transcriptional and posttranscriptional levels in a murine ***bone*** marrow stromal cell line.

AU Derigs, H. Guenter [Reprint author]; Reifel-Miller, Anne; Kaushansky, Kenneth; Hromas, Robert A.; Boswell, H. Scott

CS Div. Hematology, Third Dep. Med., Johannes Gutenberg-Univ., Langenbeckstrasse 1, 55101 Mainz, Germany

SO Experimental Hematology (Charlottesville), (1994) Vol. 22, No. 9, pp. 932-932.

CODEN: EXHMA6. ISSN: 0301-472X.

DT Article

LA English

ED Entered STN: 11 Oct 1994

Last Updated on STN: 12 Oct 1994

AB We have reported modulation, by cytokines interleukin-1-beta production stimulated by IL-1 or by the synergistic stimulus granulocyte-macrophage colony-stimulatory factor (GM-CSF) of IL-1 plus TNF-alpha. On the other hand, increased intracellular cAMP stimulated IL-6 synthesis in +/+1.LDA11 cells. In addition, cAMP was additive with either IL-1 or IL-1 plus TNF-alpha in inducing production of soluble IL-6. In the present study, these observations were pursued mechanistically at the level of messenger RNA (mRNA) production. Northern blot analysis of steady-state mRNA for GM-CSF revealed induction by treatment of +/+1.LDA11 cells with IL-1 or with TNF-alpha. The combined stimulation by IL-1 plus TNF-alpha resulted in supra-additive increases in GM-CSF expression by +/+1.LDA11. Addition to stromal cells of the soluble cAMP agonist 8-bromo-cAMP (8BrcAMP) at 0.5 to 1 mM stimulated IL-6 mRNA expression acting alone, and it was additive with IL-1 or IL-1 plus TNF-alpha in stimulating IL-6 expression. On the other hand, 8BrcAMP inhibited GM-CSF mRNA expression stimulated by IL-1 or IL-1 plus TNF-alpha. Inhibition of GM-CSF mRNA by 8BrcAMP was time-dependent, starting 120 to 180 minutes posttreatment. In addition, inhibition of GM-CSF transcript expression in +/+1.LDA11 by 8BrcAMP required the expression of a labile protein. Nuclear run-on assays revealed that GM-CSF and IL-6 genes were transcriptionally induced in +/+1.LDA11 by incubation with IL-1 plus TNF-alpha. IL-6 transcription was further enhanced by 8BrcAMP co-incubation. More sensitive experiments using a luciferase reporter ***vector*** containing the ***GM*** - ***CSF*** promoter region were necessary to convincingly establish the role of TNF-alpha and 8BrcAMP on transcriptional induction of the GM-CSF gene in +/+1.LDA11 stromal cells. Considering these results and an effect of 8BrcAMP on decreasing GM-CSF transcript stability in actinomycin-D (act-D) decay experiments, we conclude that the inhibitory effect of 8BrcAMP on GM-CSF expression is exerted at the

posttranscriptional level. These data demonstrate that the intracellular level of cAMP has an important discriminatory role on expression of the cytokines GM-CSF and IL-6 in a model stromal cell line.

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AN 94257385 EMBASE <<LOGINID::20070126>>
DN 1994257385

TI Granulocyte-macrophage colony-stimulating factor expression is regulated at transcriptional and posttranscriptional levels in a murine ***bone*** marrow*** stromal cell line.

AU Derigs H.G.; Reifel-Miller A.; Kaushansky K.; Hromas R.A.; Boswell H.S.
CS Division of Hematology, Third Department of Medicine, Johannes Gutenberg-Universität, Langenbeckstrasse 1, 55101 Mainz, Germany
SO Experimental Hematology, (1994) Vol. 22, No. 9, pp. 924-932. .
ISSN: 0301-472X CODEN: EXHEBH

CY United States
DT Journal; Article
FS .022 Human Genetics
025 Hematology
037 Drug Literature Index

LA English
SL English
ED Entered STN: 21 Sep 1994
Last Updated on STN: 21 Sep 1994

AB We have reported modulation by cytokines interleukin-1.beta. (IL-1.beta.) and tumor necrosis factor-alpha. (TNF-alpha.) and by hormonal cyclic-adenosine-monophosphate (cAMP) agonists, of hematopoietic growth factor production in the murine marrow adherent cell line +/-1.LDA11. Previously, we reported that increased intracellular cAMP levels inhibited bioactive granulocyte-macrophage colony-stimulatory factor (GM-CSF) production stimulated by IL-1 or by the synergistic stimulus of IL-1 plus TNF-alpha.. On the other hand, increased intracellular cAMP stimulated IL-6 synthesis in +/-1.LDA11 cells. In addition, cAMP was additive with either IL-1 or IL-1 plus TNF-alpha. in inducing production of soluble IL-6. In the present study, these observations were pursued mechanistically at the level of messenger RNA (mRNA) production. Northern blot analysis of steady-state mRNA for GM-CSF revealed induction by treatment of +/-1.LDA11 cells with IL-1 or with TNF-alpha.. The combined stimulation by IL-1 plus TNF-alpha. resulted in supra-additive increases in GM-CSF expression by +/-1.LDA11. Addition to stromal cells of the soluble cAMP agonist 8-bromo-cAMP (8BrCAMP) at 0.5 to 1 mM stimulated IL-6 mRNA expression acting alone, and it was additive with IL-1 or IL-1 plus TNF-alpha. in stimulating IL-6 expression. On the other hand, 8BrCAMP inhibited GM-CSF mRNA expression stimulated by IL-1 or IL-1 plus TNF-alpha.. Inhibition of GM-CSF mRNA by 8BrCAMP was time-dependent, starting 120 to 180 minutes posttreatment. In addition, inhibition of GM-CSF transcript expression in +/-1.LDA11 by 8BrCAMP required the expression of a labile protein. Nuclear run-on assays revealed that GM-CSF and IL-6 genes were transcriptionally induced in +/-1.LDA11 by incubation with IL-1 plus TNF-alpha.. IL-6 transcription was further enhanced by 8BrCAMP co-incubation. More sensitive experiments using a luciferase reporter ***vector*** containing the ***GM*** - ***CSF*** promoter region were necessary to convincingly establish the role of TNF-alpha. and 8BrCAMP on transcriptional induction of the GM-CSF gene in +/-1.LDA11 stromal cells. Considering these results and an effect of 8BrCAMP on decreasing GM-CSF transcript stability in actinomycin-D (act-D) decay experiments, we conclude that the inhibitory effect of 8BrCAMP on GM-CSF expression is exerted at the posttranscriptional level. These data demonstrate that the intracellular level of cAMP has an important discriminatory role on expression of the cytokines GM-CSF and IL-6 in a model stromal cell line.

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AN 94105618 EMBASE <<LOGINID::20070126>>
DN 1994105618

TI Regulation of interleukin-1 and tumor necrosis factor-alpha. induced granulocyte-macrophage colony-stimulating factor gene expression: Potential involvement of arachidonic acid metabolism.

AU Rizzo M.T.; Boswell H.S.
CS Division of Hematology/Oncology, Medical Research/Library Building, Indiana University Medical Center, 975 W. Walnut Street, Indianapolis, IN 46202, United States
SO Experimental Hematology, (1994) Vol. 22, No. 1, pp. 87-94. .
ISSN: 0301-472X CODEN: EXHEBH

CY United States
DT Journal; Article
FS 025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index

LA English
SL English
ED Entered STN: 4 May 1994
Last Updated on STN: 4 May 1994

AB Signal transduction pathways evoked by interleukin-1 (IL-1) and tumor necrosis factor-alpha. (TNF-alpha.) to stimulate expression of other cytokines in mesenchymal cells are not clearly understood. Stimulation of the murine ***bone*** marrow*** stromal cell line +/-LLDA 11 with IL-1 (500 U/ml) in combination with TNF-alpha. (500 U/ml) (IL-1 plus TNF-alpha.) induced expression of c-jun mRNA as well as granulocyte-macrophage colony stimulating factor (GM-CSF) mRNA. We

investigated the possibility that arachidonic acid metabolites, acting through protein kinase C (PKC) and perhaps also through the PKC-responsive transcription factor c-jun/AP-1, may be responsible for regulating GM-CSF transcription in these stromal cells. Expression of GM-CSF mRNA was preceded by IL-1 plus TNF-alpha. induced arachidonate release (assayed using the 3H- derivative). Pretreatment of cells with the phospholipase A2 inhibitor quinacrine (20 .mu.M) inhibited accumulation of both c-jun and GM-CSF mRNA, but had no influence on expression of other genes

induced by IL-1 and TNF-alpha., including leukemia inhibitory factor (LIF). In addition, quinacrine partially blocked IL-1 plus TNF-alpha. induced 3H-arachidonic acid release from prelabeled stromal cells. Furthermore, exogenous arachidonate (10 to 50 .mu.M) induced expression of c-jun. To investigate the role of arachidonate in ***GM*** - ***CSF*** transcription, we used a reporter ***vector*** consisting of the murine ***GM*** - ***CSF*** promoter linked to firefly luciferase. Transfection efficiency was monitored by assessing expression of a constitutively active gene, RSV-beta. galactosidase. In this system, quinacrine significantly inhibited IL-1 plus TNF-alpha. induced GM-CSF transcription assayed with the reporter construct. Exogenous arachidonic acid alone (10 .mu.M) increased activity of ***GM*** - ***CSF*** reporter ***vector*** 1.5-fold over control. These results are consistent with the hypothesis that arachidonate metabolites are involved in the signaling pathway that leads to IL-1 plus TNF-alpha. induced GM-CSF gene expression. Thus, transcriptional activation of GM-CSF gene is mediated, in part, by the arachidonate cascade.

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=> s angiogen? or (blood vessel (3a) form?)
L9 119582 ANGIOGEN? OR (BLOOD VESSEL (3A) FORM?)

=> d his

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FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 16:53:37 ON 26 JAN 2007
L1 369490 S BONE MARROW
L2 12787 S L1 AND (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR EPAS1 OR M
L3 26915 S ADENOVIR? (3A) VECTOR
L4 54 S L2 AND L3
L5 50 DUP REM L4 (4 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:04:32 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:23:19 ON 26 JAN 2007
L6 951 S VECTOR (7A) (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR EPAS1
L7 39 S L1 AND L6
L8 26 DUP REM L7 (13 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:33:18 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:39:31 ON 26 JAN 2007
L9 119582 S ANGIOGEN? OR (BLOOD VESSEL (3A) FORM?)

=> s l1 and l9
L10 4578 L1 AND L9

=> s l2 and l10
L11 374 L2 AND L10

=> s l2 and l9
L12 374 L2 AND L9

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 292 DUP REM L12 (82 DUPLICATES REMOVED)

=> s l13 and py<=2003
L14 136 L13 AND PY<=2003

=> d bib abs 1-10

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AN 2004508330 EMBASE <<LOGINID::20070126>>

TI Divergent effects of ***GM*** - ***CSF*** and TGF.β(1) on
bone ***marrow***-derived macrophage arginase-1 activity,
MCP - ***1*** expression, and matrix metalloproteinase-12: A
potential role during arteriogenesis.

AU Jost M.M.; Ninci E.; Meder B.; Kempf C.; Van Royen N.; Hua T.; Berger B.;
Hoefler I.; Modolell M.; Buschmann I.

CS M.M. Jost, Res. Grp. Exp./Clin. Angiogenesis, Department for Internal
Medicine III, Albert-Ludwigs University Freiburg, Breisacher Strasse 66
(ZKF), D-79106 Freiburg im Breisgau, Germany. meyer@medl.ukl.uni-
freiburg.de

SO FASEB Journal, (2003) Vol. 17, No. 15, pp. 2281-2283.
ISSN: 0892-6638 CODEN: FAJOEC

CY United States
DT Journal; Article
FS 025 Hematology
029 Clinical Biochemistry

LA English
ED Entered STN: 17 Dec 2004
Last Updated on STN: 17 Dec 2004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L14 ANSWER 2 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2004078595 EMBASE <<LOGINID::20070126>>

TI [Hypoxia and ***angiogenesis*** in rheumatic diseases].
HYPOXIE UND ***ANGIOGENESE*** IN RHEUMATISCHEN
ERKRANKUNGEN.

AU Distler O.

CS Dr. O. Distler, Zentrum Experimentelle Rheumatol., Universitätsklinik
Zurich, Gloriastr. 25, 8091 Zurich, Switzerland. Oliver.Distler@usz.ch

SO Zeitschrift für Rheumatologie, Supplement, (2003) Vol. 62, No. 2, pp.
1143-1145.
Refs: 12
ISSN: 0941-8466 CODEN: ZRSEAM

CY Germany
DT Journal; Conference Article
FS 005 General Pathology and Pathological Anatomy
031 Arthritis and Rheumatism

LA German
SL English; German
ED Entered STN: 4 Mar 2004
Last Updated on STN: 4 Mar 2004

AB The important role of ***angiogenesis*** for the pathogenesis of most
tumors has gained much interest into the mechanisms of new vessel
formation during recent years. Hypoxia induces ***angiogenesis*** via
stabilization of the transcription factor ***HIF*** -1.α. After
dimerization of ***HIF*** -1.α with ***HIF*** -1.β/ARNT,
HIF -1 binds to the hypoxia-responsive elements in the regulatory
regions of proangiogenic molecules such as VEGF. Hypoxia-mediated
angiogenesis also plays a part in the pathogenesis of rheumatoid
arthritis. For instance, intraarticular application of the angiostatic
molecule angiostatin reduces the severity of collagen-induced arthritis in
mice. Moreover, recent data indicate that the expression of ***HIF***
-1.α in myeloid cells is important for the initiation of the
inflammatory infiltrate in rheumatoid arthritis. In contrast to
rheumatoid arthritis, the therapeutic goal in systemic sclerosis (SSc) is
the formation of new vessels rather than the inhibition of
angiogenesis. Surprisingly, several proangiogenic factors such as
VEGF or ***MCP*** - ***1*** (CCL-2) are overexpressed in the skin of
patients with SSc despite the reduction in the capillary density. The
role of these findings for the defective ***angiogenesis*** in SSc is
currently investigated in our laboratory.

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AN 2003479716 EMBASE <<LOGINID::20070126>>

TI Carcinoid: A Comprehensive Review.

AU Schnirer I.J.; Yao J.C.; Ajani J.A.

CS J.A. Ajani, Department of GI Oncology, Box 78, Univ. TX M. D. Anderson

Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77005-4341, United States.
Jajani@mdanderson.org

SO Acta Oncologica, (2003) Vol. 42, No. 7, pp. 672-692.
Refs: 248

ISSN: 0284-186X CODEN: ACTOEL

CY Norway

DT Journal; General Review

FS 003 Endocrinology

008 Neurology and Neurosurgery

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 11 Dec 2003

Last Updated on STN: 11 Dec 2003

AB Carcinoid tumors originate from the neuroendocrine cells throughout the
body and are capable of producing various peptides. Their clinical course
is often indolent but can also be aggressive and resistant to therapy. We
examined all aspects of carcinoid tumors including the molecular biology
oncogenesis, role of ***angiogenesis***, recent advances in imaging,
and therapy. The Medline and Cancerlit databases were searched using
carcinoid as the keyword. English language manuscripts were reviewed and
relevant references from a total of 7 741 were found. All titles were
screened and all the relevant manuscripts were analyzed; we found 307
references pertinent to the history, epidemiology, clinical behavior,
pathology, pathophysiology, molecular biology, radiologic imaging,
supportive care of carcinoid syndrome, and results of therapeutic clinical
trials. Management of patients with carcinoid tumors requires an
understanding of the disease process and a multimodality approach.
Introduction of long-acting somatostatin analogues has resulted in
significant advances in the palliative care of patients with carcinoid
syndrome. However, advanced carcinoid tumor remains incurable. Existing
therapies for advanced disease have low biologic activity, high toxicity,
or both. Clearly, more research is necessary in the areas of molecular
biology, targeted therapy, and development of new drugs. Future advances
in this field need to focus on clinical and biological predictors of
outcome. Early works in the area of tumor biology such as the role of
p53, bcl-2, bax, MEN1, ***FGF***, TGF, PDGF and VEGF expression are of
interest and need to be explored further.

L14 ANSWER 4 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2003475294 EMBASE <<LOGINID::20070126>>

TI ***Bone*** ***Marrow*** Monocyte Lineage Cells Adhere on Injured
Endothelium in a Monocyte Chemoattractant Protein-1-Dependent Manner and
Accelerate Reendothelialization as Endothelial Progenitor Cells.

AU Fujiyama S.; Amano K.; Uehira K.; Yoshida M.; Nishiwaki Y.; Nozawa Y.; Jin
D.; Takai S.; Miyazaki M.; Egashira K.; Imada T.; Iwasaka T.; Matsubara H.
CS Dr. H. Matsubara, Dept. of Cardiovascular Medicine, Kyoto Pref. University
of Medicine, Kamigyo-ku, Kyoto, 602-8566, Japan. matsubah@koto.kpu-m.ac.jp

SO Circulation Research, (14 Nov 2003) Vol. 93, No. 10, pp. 980-989.
Refs: 39

ISSN: 0009-7330 CODEN: CIRUAL

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

025 Hematology

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 29 Dec 2003

Last Updated on STN: 29 Dec 2003

AB Peripheral blood (PB)-derived CD14(+) monocytes were shown to
transdifferentiate into endothelial cell (EC) lineage cells and contribute
to neovascularization. We investigated whether ***bone***
marrow (BM)- or PB-derived CD34(-)CD14(+) cells are involved in
reendothelialization after carotid balloon injury. Although neither
hematopoietic nor mesenchymal stem cells were included in human BM-derived
CD34(-)CD14(+) monocyte lineage cells (BM-MLCs), they expressed
EC-specific markers (Tie2, CD31, VE-cadherin, and endoglin) to an extent
identical to mature ECs. When BM-MLCs were cultured with vascular
endothelial growth factors, hematopoietic markers were drastically
decreased and new EC-specific markers (Flk and CD34) were induced.
BM-MLCs were intra-arterially transplanted into balloon-injured arteries
of athymic nude rats. When BM-MLCs were activated by monocyte
chemoattractant protein-1 (***MCP*** - ***1***) in vivo or in vitro,
they adhered onto injured endothelium, differentiated into EC-like cells
by losing hematopoietic markers, and inhibited neointimal hyperplasia.
Ability to prevent neointimal hyperplasia was more efficient than that of
BM-derived CD34(+) cells. MCP-dependent adhesion was not observed in
PB-derived CD34(-)CD14(+) monocytes. Regenerated endothelium exhibited
a cobblestone appearance, blocked extravasation of dye, and induced
NO-dependent vasorelaxation. Basal adhesive activities on HUVECs under
laminar flow and β(1)-integrin expression (basal and active forms)
were significantly increased in BM-MLCs compared with PB-derived
monocytes. ***MCP*** - ***1*** markedly enhanced adhesive activity
of BM-MLCs (2.8-fold) on HUVECs by activating β(1)-integrin
conformation. Thus, BM-MLCs can function as EC progenitors that are more
potent than CD34(+) cells and acquire the ability to adhere on injured
endothelium in a ***MCP*** - ***1*** -dependent manner, leading to
reendothelialization associated with inhibition of intimal hyperplasia.
This will open a novel window to ***MCP*** - ***1*** -mediated

biological actions and vascular regeneration strategies by cell therapy.

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AN 2003459279 EMBASE <<LOGINID::20070126>>

TI Testing clinical therapeutic ***angiogenesis*** using basic fibroblast growth factor (***FGF*** -2).

AU Aviles R.J.; Annex B.H.; Lederman R.J.

CS R.J. Lederman, Division of Intramural Research, Natl. Heart, Lung, and Blood Inst., National Institutes of Health, Bethesda, MD 20892-1538, United States. lederman@nih.gov

SO British Journal of Pharmacology, (2003) Vol. 140, No. 4, pp. 637-646. .

Refs: 62

ISSN: 0007-1188 CODEN: BJPCBM

CY United Kingdom

DT Journal; Conference Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 4 Dec 2003

Last Updated on STN: 4 Dec 2003

AB Therapeutic ***angiogenesis*** represents an attempt to relieve inadequate blood flow by the directed growth and proliferation of blood vessels. Neovascularization is a complex process involving multiple growth factors, receptors, extracellular matrix glycoproteins, intracellular and extracellular signaling pathways, and local and ***bone*** - ***marrow*** -derived constituent cells, all responding to a symphonic arrangement of temporal and spatial cues. In cardiovascular disease, patients with refractory angina and lower extremity intermittent claudication seem most amenable to early tests of therapeutic ***angiogenesis***. Monotherapy with the recombinant protein basic fibroblast growth factor (***FGF*** -2) has been tested in six human trials. These have shown provisional safety, and two have provided 'proof of concept' for the strategy of therapeutic ***angiogenesis***. One large randomized phase II trial failed to show significant efficacy in coronary artery disease. Another showed significant efficacy in peripheral artery disease, although the magnitude of benefit was disappointing at the dose tested. This overview details the suitable clinical trial design and further steps toward the clinical development of ***FGF*** -2.

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AN 2003288976 EMBASE <<LOGINID::20070126>>

TI Paracrine interactions of basic fibroblast growth factor and interleukin-6 in multiple myeloma.

AU Bisping G.; Leo R.; Wenning D.; Dankbar B.; Padro T.; Kropff M.; Scheffold C.; Kroger M.; Mesters R.M.; Berdel W.E.; Kienast J.

CS J. Kienast, Dept. of Med./Hematology/Oncology, University of Muenster, Albert-Schweitzer-Str 33, D-48129 Muenster, Germany. kienast@uni-muenster.de

SO Blood, (1 Apr 2003) Vol. 101, No. 7, pp. 2775-2783. .

Refs: 56

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy

016 Cancer

025 Hematology

026 Immunology, Serology and Transplantation

LA English

SL English

ED Entered STN: 10 Aug 2003

Last Updated on STN: 10 Aug 2003

AB Myeloma cells express basic fibroblast growth factor (bFGF), an ***angiogenic*** cytokine triggering marrow neovascularization in multiple myeloma (MM). In solid tumors and some lymphohematopoietic malignancies, ***angiogenic*** cytokines have also been shown to stimulate tumor growth via paracrine pathways. Since interleukin-6 (IL-6) is a potent growth and survival factor for myeloma cells, we have studied the effects of bFGF on IL-6 secretion by ***bone*** ***marrow*** stromal cells (BMSCs) and its potential reverse regulation in myeloma cells. Both myeloma-derived cell lines and myeloma cells isolated from the marrow of MM patients were shown to express and secrete bFGF. Cell-sorting studies identified myeloma cells as the predominant source of bFGF in MM marrow. BMSCs from MM patients and control subjects expressed high-affinity ***FGF*** receptors R1 through R4. Stimulation of BMSCs with bFGF induced a time- and dose-dependent increase in IL-6 secretion (median, 2-fold; $P < .001$), which was completely abrogated by anti-bFGF antibodies. Conversely, stimulation with IL-6 enhanced bFGF expression and secretion by myeloma cell lines (2-fold; $P = .02$) as well as MM patient cells (up to 3.6-fold; median, 1.5-fold; $P = .002$). This effect was inhibited by anti-IL-6 antibody. When myeloma cells were cocultured with BMSCs in a noncontact transwell system, both IL-6 and bFGF concentrations in coculture supernatants increased 2- to 3-fold over the sum of basal concentrations in the monoculture controls. The IL-6 increase was again partially, but significantly, inhibited by anti-bFGF. The data demonstrate a paracrine interaction between myeloma and marrow stromal cells triggered by mutual stimulation of bFGF and IL-6. COPYRIGHT. 2003 by The American Society of Hematology.

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AN 2003009122 EMBASE <<LOGINID::20070126>>

TI [Cell transplants and gene therapy. New methods of treatment of post-infarction circulatory insufficiency].

PRZESZCZEPY KOMORKOWE I TERAPIA GENOWA. NOWE METODY

LECZENIA POZAWAJOWEJ

NIEWYDOLNOSCI KRAZENIA.

AU Rozwadowska N.; Fiszer D.; Siminiak T.; Kalawski R.; Kurpisz M.

CS Prof. M. Kurpisz, Zakład Genetyki Człowieka Pan, ul. Strzeszyńska 32, 60-479 Poznań, Poland. kurpimac@man.poznan.pl

SO Polski Przegląd Kardiologiczny, (2002) Vol. 4, No. 4, pp. 325-329. .

Refs: 29

ISSN: 1507-5540 CODEN: PPKOAO

CY Poland

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

022 Human Genetics

037 Drug Literature Index

LA Polish

SL Polish; English

ED Entered STN: 16 Jan 2003

Last Updated on STN: 16 Jan 2003

AB The number of cases of post-infarction circulatory insufficiency is still on rise and presently employed forms of therapy do not directly access to the pathologically malformed tissue. The proposed, new therapeutic attempt is based on cellular engineering and gene therapy or combination of both. So far, there have been proposed autologous ***bone*** ***marrow*** cells, fibroblasts, myoblasts or kardiomyocytes as the source of tissue transplants to the post-infarction scar. Gene therapy is based upon administration of constructs containing genes connected with ***angiogenic*** process: VEGF (vascular endothelial growth factor), bFGF/FGF2 (basic fibroblast growth factor), PDGF-BB (platelet-derived growth factor) and ***HIF*** -1 alpha (hypoxia-inducible factor-1 alpha). As well cellular engineering as gene therapy were studied first in animal models. Majority of protocols were successful therefore phase I clinical trials began; at present even phase II clinical trials have been initiated. Collection of the data will allow to optimize a therapy and perhaps will deliver to patients and physicians a long awaited solution, i.e. successful treatment of increasing cases of post-infarction circulatory insufficiency. A present review summarizes new methods of treatment of post-infarcted heart.

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AN 2002408427 EMBASE <<LOGINID::20070126>>

TI BCR/ABL induces expression of vascular endothelial growth factor and its transcriptional activator, hypoxia inducible factor-1 alpha., through a pathway involving phosphoinositide 3-kinase and the mammalian target of rapamycin.

AU Mayerhofer M.; Valent P.; Sperr W.R.; Griffin J.D.; Sillaber C.

CS C. Sillaber, Department of Internal Medicine I, University of Vienna, AKH-Wien, Wahringer Gurtel 18-20, A-1097 Vienna, Austria. christian.sillaber@univie.ac.at

SO Blood, (15 Nov 2002) Vol. 100, No. 10, pp. 3767-3775. .

Refs: 59

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 016 Cancer

022 Human Genetics

025 Hematology

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 5 Dec 2002

Last Updated on STN: 5 Dec 2002

AB Recent data suggest that vascular endothelial growth factor (VEGF), a cytokine involved in autocrine growth of tumor cells and tumor ***angiogenesis***, is up-regulated and plays a potential role in myelogenous leukemias. In chronic myelogenous leukemia (CML), VEGF is expressed at high levels in the ***bone*** ***marrow*** and peripheral blood. We show here that the CML-associated oncogene BCR/ABL induces VEGF gene expression in growth factor-dependent Ba/F3 cells. Whereas starved cells were found to contain only baseline levels of VEGF mRNA, Ba/F3 cells induced to express BCR/ABL exhibited substantial amounts of VEGF mRNA. BCR/ABL also induced VEGF promoter activity and increased VEGF protein levels in Ba/F3 cells. Moreover, BCR/ABL was found to promote the expression of functionally active hypoxia-inducible factor-1 (***HIF*** -1), a major transcriptional regulator of VEGF gene expression. BCR/ABL-induced VEGF gene expression was counteracted by the phosphoinositide 3-kinase (PI3-kinase) inhibitor LY294002 and rapamycin, an antagonist of mammalian target of rapamycin (mTOR), but not by inhibition of the mitogen-activated protein kinase pathway. Similarly, BCR/ABL-dependent ***HIF*** -1.alpha. expression was inhibited by the addition of LY294002 and rapamycin. Together, our data show that BCR/ABL induces VEGF- and ***HIF*** -1.alpha. gene expression through a pathway involving PI3-kinase and mTOR. BCR/ABL-induced VEGF expression may contribute to the pathogenesis and increased ***angiogenesis*** in CML. COPYRIGHT. 2002 by The American Society of Hematology.

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AN 2002348406 EMBASE <<LOGINID::20070126>>

TI Basic fibroblast growth factor stimulates osteoclast recruitment, development, and bone pit resorption in association with ***angiogenesis*** in vivo on the chick chorioallantoic membrane and activates isolated avian osteoclast resorption in vitro.

AU Collin-Osdoby P.; Rothe L.; Bekker S.; Anderson F.; Huang Y.; Osdoby P.

CS Dr. P. Collin-Osdoby, Department of Biology, Box 1229, Washington University, St. Louis, MO 63130, United States

SO Journal of Bone and Mineral Research, (1 Oct 2002) Vol. 17, No. 10, pp. 1859-1871.

Refs: 69

ISSN: 0884-0431 CODEN: JBMREJ

CY United States

DT Journal; Article

FS 021 Developmental Biology and Teratology

029 Clinical Biochemistry

033 Orthopedic Surgery

037 Drug Literature Index

LA English

SL English

ED Entered STN: 17 Oct 2002

Last Updated on STN: 17 Oct 2002

AB Increased local osteoclast (OC)-mediated bone resorption coincides with ***angiogenesis*** in normal bone development and fracture repair, as well as in pathological disorders such as tumor-associated osteolysis and inflammatory-related rheumatoid arthritis or periodontal disease.

Angiogenic stimulation causes recruitment, activation, adhesion, transmigration, and differentiation of hematopoietic cells which may therefore enable greater numbers of pre-OC to emigrate from the circulation and develop into bone-resorptive OCs. A chick chorioallantoic membrane (CAM) model, involving coimplantation of a stimulus in an agarose plug directly adjacent to a bone chip was used to investigate if a potent ***angiogenic*** stimulator, basic fibroblast growth factor (bFGF), could promote OC recruitment, differentiation, and resorption in vivo.

Angiogenesis elicited by bFGF on the CAM was accompanied by increased OC formation and bone pit resorption (both overall and on a per OC basis) on the bone implants in vivo. In complementary in vitro assays, bFGF did not directly stimulate avian OC development from ***bone*** ***marrow*** mononuclear cell precursors, consistent with their low mRNA expression of the four avian signaling ***FGF*** receptors (FGFR)-1, FGFR-2, FGFR-3, and FGFR-like embryonic kinase (FREK). In contrast, bFGF activated isolated avian OC bone pit resorption via mechanisms inhibited by a selective cyclo-oxygenase (COX)-2 prostaglandin inhibitor (NS-398) or p42/p44 MAPK activation inhibitor (PD98059), consistent with a relatively high expression of FGFR-1 by differentiated avian OCs. Thus, bFGF may sensitively regulate local bone resorption and remodeling through direct and indirect mechanisms that promote ***angiogenesis*** and OC recruitment, formation, differentiation, and activated bone pit resorption. The potential for bFGF to coinduce ***angiogenesis*** and OC bone remodeling may find clinical applications in reconstructive surgery, fracture repair, or the treatment of avascular necrosis. Alternatively, inhibiting such bFGF-dependent processes may aid in the treatment of inflammatory-related or metastatic bone loss.

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AN 2002234417 EMBASE <<LOGINID::20070126>>

TI [***Angiogenesis*** in patients with hematologic malignancies]. ***ANGIOGENESE*** BEI HAMATOLOGISCHEN NEOPLASIEN.

AU Mesters R.M.; Padro T.; Steins M.; Bieker R.; Retzlaff S.; Kessler T.; Kienast J.; Berdel W.E.

CS Dr. R.M. Mesters, Medizinische Klinik und Poliklinik A, Universitätsklinikum Munster, Albert-Schweitzer-Strasse 33, D-48129 Munster, Germany. mesters@uni-muenster.de

SO Onkologie, (2001) Vol. 24, No. SUPPL. 5, pp. 75-80.

Refs: 44

ISSN: 0378-584X CODEN: ONKOD2

CY Germany

DT Journal; Conference Article

FS 005 General Pathology and Pathological Anatomy

016 Cancer

025 Hematology

030 Pharmacology

037 Drug Literature Index

LA German

SL English; German

ED Entered STN: 11 Jul 2002

Last Updated on STN: 11 Jul 2002

AB The importance of ***angiogenesis*** for the progressive growth and viability of solid tumors is well established. Emerging data suggest an involvement of ***angiogenesis*** in the pathophysiology of hematologic malignancies as well. Recently, we and others have reported increased ***angiogenesis*** in the ***bone*** ***marrow*** of patients with acute myeloid leukemia (AML) and normalization of ***bone*** ***marrow*** microvessel density when patients achieved a complete remission (CR) after induction chemotherapy. Tumor ***angiogenesis*** depends on the expression of specific mediators that initiate a cascade of events leading to the formation of new microvessels. Among these, VEGF (vascular endothelial growth factor), ***FGF*** (fibroblast growth factor) and angiopoietins play a pivotal role in the induction of neovascularization in solid tumors. These cytokines

stimulate migration and proliferation of endothelial cells and induce ***angiogenesis*** in vivo. Recent data suggest an important role for these mediators in hematologic malignancies as well. Isolated AML blasts overexpress VEGF and VEGF receptor 2. Thus, the VEGF/VEGFR-2 pathway can

promote the growth of leukemic blasts in an autocrine and paracrine manner. Therefore, neovascularization and ***angiogenic*** mediators/receptors may be promising targets for anti- ***angiogenic*** and anti-leukemic treatment strategies. The immunomodulatory drug thalidomide inhibits ***angiogenesis*** in animal models. Moreover, it has significant activity in refractory multiple myeloma. In a current phase II study for patients with primary refractory or relapsed multiple myeloma using a combination of thalidomide with hyperfractionated cyclophosphamide and dexamethasone (Hyper-CDT), we observed a partial remission in 12 of 14 evaluable patients (86%). Thus, this combination seems to be very potent. Furthermore, we evaluated the safety and efficacy of thalidomide in patients with AML not qualifying for intensive cytotoxic chemotherapy. 20 patients aged 58-85 (median 69) years were recruited to this phase I/II study and were treated with a dose of 200-400 mg per os daily for a duration of 1-40 (median 6) weeks, dependent on the individual tolerability of the drug. In 4 patients we observed a partial response (PR - defined as more than 50% reduction in leukemic blast infiltration in the ***bone*** ***marrow***). This was accompanied by an increase in platelet counts and hemoglobin values. One additional patient showed a significant improvement of peripheral blood counts without fulfilling the criteria of a PR. In parallel, we observed a significant decrease in microvessel density in these 5 patients during treatment with thalidomide. In conclusion, thalidomide seems to have anti- ***angiogenic*** as well as anti-leukemic activity in AML. The VEGF/VEGFR-2 pathway seems to play an important role in AML. Therefore, receptor tyrosine kinase inhibitors like SU5416 or SU6668 are currently evaluated in the context of phase II studies in AML. We could recently induce a stable remission in a patient with second relapse of her AML refractory towards chemotherapy by administration of SU5416 (compassionate use), a tyrosine kinase inhibitor of VEGFR-2 and c-kit. Current and future studies will clarify the role of anti- ***angiogenic*** treatment strategies in AML and other hematologic malignancies.

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TOTAL	ENTRY	SESSION
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L1 369490 S BONE MARROW
L2 12787 S L1 AND (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR
EPAS1 OR M
L3 26915 S ADENOVIR? (3A) VECTOR
L4 54 S L2 AND L3
L5 50 DUP REM L4 (4 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:04:32 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:23:19 ON 26 JAN 2007
L6 951 S VECTOR (7A) (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1
OR EPAS1
L7 39 S L1 AND L6
L8 26 DUP REM L7 (13 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:33:18 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:39:31 ON 26 JAN 2007
L9 119582 S ANGIOGEN? OR (BLOOD VESSEL (3A) FORM?)
L10 4578 S L1 AND L9
L11 374 S L2 AND L10
L12 374 S L2 AND L9
L13 292 DUP REM L12 (82 DUPLICATES REMOVED)
L14 136 S L13 AND PY<=2003

FILE 'STNGUIDE' ENTERED AT 17:46:26 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:51:06 ON 26 JAN 2007

=> s l13 and (heart or myocard? or limb or ischemia)
L15 99 L13 AND (HEART OR MYOCARD? OR LIMB OR ISCHEMIA)

=> d bib abs 1-20

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AN 2006554101 EMBASE <<LOGINID:20070126>>

TI Physical activity improves long-term stroke outcome via endothelial nitric oxide synthase-dependent augmentation of neovascularization and cerebral blood flow.

AU Gertz K.; Priller J.; Kronenberg G.; Fink K.B.; Winter B.; Schrock H.; Ji S.; Milosevic M.; Harms C.; Bohm M.; Dirmagl U.; Laufs U.; Endres M.
CS Dr. Prof. M. Endres, Charite-Universitätsmedizin Berlin, Department of Neurology, Schumannstr. 20/21, 10117 Berlin, Germany.
matthias.endres@charite.de

SO Circulation Research, (2006) Vol. 99, No. 10, pp. 1132-1140. .
Refs: 29

ISSN: 0009-7330 CODEN: CIRUAL

PUI 0000301220061110000016

CY United States

DT Journal; Article

FS 008 Neurology and Neurosurgery

018 Cardiovascular Diseases and Cardiovascular Surgery

LA English

SL English

ED Entered STN: 28 Nov 2006

Last Updated on STN: 28 Nov 2006

AB Physical activity upregulates endothelial nitric oxide synthase (eNOS), improves endothelium function, and protects from vascular disease. Here, we tested whether voluntary running would enhance neovascularization and long-term recovery following mild brain ***ischemia***. Wild-type mice were exposed to 30 minutes of middle-cerebral artery occlusion (MCAO) and reperfusion. Continuous voluntary running on wheels conferred long-term upregulation of eNOS in the vasculature and of endothelial progenitor cells (EPCs) in the spleen and ***bone*** marrow*** (BM). This was associated with higher numbers of circulating EPCs in the blood and enhanced neovascularization. Moreover, engraftment of Tie2/LacZ-positive BM-derived cells was increased in the ischemic brain. Four weeks after the insult, trained animals showed higher numbers of newly generated cells in vascular sites, increased density of perfused microvessels and sustained augmentation of cerebral blood flow within the ischemic striatum. Moreover, running conferred tissue sparing and improved functional outcome at 4 weeks. The protective effects of running on ***angiogenesis*** and outcome were completely abolished when animals were treated with a ***NOS*** inhibitor or the antiangiogenic compound endostatin after brain ***ischemia***, and in animals lacking eNOS expression. Voluntary physical activity improves long-term stroke outcome by eNOS-dependent mechanisms related to improved ***angiogenesis*** and cerebral blood flow. .COPYRG. 2006 American ***Heart*** Association, Inc.

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AN 2006418692 EMBASE <<LOGINID:20070126>>

TI ***Angiogenic*** murine endothelial progenitor cells are derived from a myeloid ***bone*** marrow*** fraction and can be identified by endothelial NO synthase expression.

AU Loomans C.J.M.; Wan H.; De Crom R.; Van Haperen R.; De Boer H.C.; Leenen

P.J.M.; Drexhage H.A.; Rabelink T.J.; Van Zonneveld A.J.; Staal F.J.T.

CS Dr. F.J.T. Staal, Department of Immunology, Erasmus MC, Dr Molewaterplein 50, 3015GE Rotterdam, Netherlands. f.staal@erasmusmc.nl

SO Arteriosclerosis, Thrombosis, and Vascular Biology, (2006) Vol. 26, No. 8, pp. 1760-1767. .

Refs: 47

ISSN: 1079-5642 CODEN: ATVBFA

PUI 0004360520060800000013

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

025 Hematology

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 8 Sep 2006

Last Updated on STN: 8 Sep 2006

AB OBJECTIVE - Endothelial progenitor cells (EPCs) contribute to postnatal neovascularization and are therefore of great interest for autologous cell therapies to treat ischemic vascular disease. However, the origin and functional properties of these EPCs are still in debate. METHODS AND RESULTS - Here, ex vivo expanded murine EPCs were characterized in terms of phenotype, lineage potential, differentiation from ***bone*** marrow*** (BM) precursors, and their functional properties using endothelial NO synthase (eNOS)-green fluorescent protein transgenic mice. Despite high phenotypic overlap with macrophages and dendritic cells, EPCs displayed unique eNOS expression, endothelial lineage potential in colony assays, and ***angiogenic*** characteristics, but also immunologic properties such as interleukin-12p70 production and low levels of T-cell stimulation. The majority of EPCs developed from an immature, CD31 (+)Ly6C(+) myeloid progenitor fraction in the BM. Addition of myeloid growth factors such as macrophage-colony-stimulating factor (M-CSF) and granulocyte/macrophage (***GM***)-***CSF*** stimulated the expansion of spleen-derived EPCs but not BM-derived EPCs. CONCLUSION: The close relationship between EPCs and other myeloid lineages may add to the complexity of using them in cell therapy. Our mouse model could be a highly useful tool to characterize EPCs functionally and phenotypically, to explore the origin and optimize the isolation of EPC fractions for therapeutic neovascularization. .COPYRG. 2006 American ***Heart*** Association, Inc.

L15 ANSWER 3 OF 99 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

AN 2006415393 EMBASE <<LOGINID:20070126>>

TI Synthetic vascular prosthesis impregnated with mesenchymal stem cells overexpressing endothelial nitric oxide synthase.

AU Kanki-Horimoto S.; Horimoto H.; Mieno S.; Kishida K.; Watanabe F.; Furuya E.; Katsumata T.

CS Dr. S. Kanki-Horimoto, Department of Thoracic and Cardiovascular Surgery, Osaka Medical College, 2-7 Daigakumachi Takatsuki, Osaka, 569-8686, Japan. tho064@poh.osaka-med.ac.jp

SO Circulation, (2006) Vol. 114, No. SUPPL. 1, pp. I327-I330. .

Refs: 14

ISSN: 0009-7322 CODEN: CIRCAZ

PUI 0000301720060704100053

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

022 Human Genetics

027 Biophysics, Bioengineering and Medical Instrumentation

030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 7 Sep 2006

Last Updated on STN: 7 Sep 2006

AB BACKGROUND - Endothelial dysfunction is known to exaggerate coronary artery disease, sometimes leading to irreversible ***myocardial*** damage. In such cases, repetitive coronary revascularization including coronary artery bypass grafting is needed, which may cause a shortage of graft conduits. On the other hand, endothelial nitric oxide synthase (eNOS) is an attractive target of cardiovascular gene therapy. The vascular prostheses, of which the inner surfaces are covered with mesenchymal stem cells (MSCs) overexpressing eNOS, are expected to offer feasible effects of NO and ***angiogenic*** effects of MSCs on the native coronary arterial beds, as well as improvement of self-patency. Herein, we attempted to develop small caliber vascular prostheses generating the bioactive proteins. Also, we attempted to transduce eNOS cDNA into MSCs. METHODS AND RESULTS - The MSCs were isolated from rat

bone marrow*** and transduced with each adenovirus harboring rat eNOS cDNA and .beta.-galactosidase (.beta.-gal) (eNOS/MSCs and .beta.-gal/MSCs). The .beta.-gal/MSCs were impregnated into vascular prostheses, then the expressions of .beta.-gal on the inner surfaces of them were evaluated by 5-bromo-4-chloro-3-indolyl .beta.-d-galactoside staining. The ***NOS*** activity of eNOS/MSCs was assayed by monitoring the conversion of H-arginine to H-citrulline. The inner surfaces of the vascular prostheses were covered with MSCs expressing .beta.-gal. The amount of the H-citrulline increased, and eNOS/MSCs were determined to generate enzymatic activity of eNOS. This activity was completely inhibited by N-nitro-L-arginine methyl ester. CONCLUSIONS - The inner surface of expanded polytetrafluoroethylene vascular prostheses seeded with lacZ gene-transduced MSCs exhibited recombinant proteins. Development of eNOS/MSC-seeded vascular prostheses would promise much longer graft patency and vasculoprotective effects. .COPYRG. 2006 American ***Heart*** Association, Inc.

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AN 2005344631 EMBASE <<LOGINID:20070126>>

TI Stromal cell-derived factor and granulocyte-monocyte colony-stimulating factor form a combined neovascularogenic therapy for ischemic cardiomyopathy.

AU Woo Y.J.; Grand T.J.; Berry M.F.; Altun P.; Moise M.A.; Hsu V.M.; Cohen J.; Fisher O.; Burdick J.; Taylor M.; Zentko S.; Liao G.; Smith M.; Kolakowski S.; Jayasankar V.; Gardner T.J.; Sweeney H.L.

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SO Journal of Thoracic and Cardiovascular Surgery, (2005) Vol. 130, No. 2, pp. 321-329.

Refs: 29

ISSN: 0022-5223 CODEN: JTCSAQ

PUI S 0022-5223(04)01705-2

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

037 Drug Literature Index

LA English

SL English

ED Entered STN: 1 Sep 2005

Last Updated on STN: 1 Sep 2005

AB Objective: Ischemic ***heart*** failure is an increasingly prevalent global health concern with major morbidity and mortality. Currently, therapies are limited, and novel revascularization methods might have a role. This study examined enhancing endogenous ***myocardial*** revascularization by expanding ***bone*** ***marrow*** derived endothelial progenitor cells with the marrow stimulant granulocyte-monocyte colony-stimulating factor and recruiting the endothelial progenitor cells with intramyocardial administration of the potent endothelial progenitor cell chemokine stromal cell-derived factor. Methods: Ischemic cardiomyopathy was induced in Lewis rats (n = 40) through left anterior descending coronary artery ligation. After 3 weeks, animals were randomized into 4 groups: saline control, granulocyte-monocyte colony-stimulating factor only (***GM*** - ***CSF*** only), stromal cell-derived factor only (SDF only), and combined stromal cell-derived factor/granulocyte-monocyte colony-stimulating factor (SDF/ ***GM*** - ***CSF***) (n = 10 each). After another 3 weeks, hearts were analyzed for endothelial progenitor cell density by endothelial progenitor cell marker colocalization immunohistochemistry, vasculogenesis by von Willebrand immunohistochemistry, ventricular geometry by hematoxylin-and-eosin microscopy, and in vivo ***myocardial*** function with an intracavitary pressure-volume conductance microcatheter. Results: The saline control, ***GM*** - ***CSF*** only, and SDF only groups were equivalent. Compared with the saline control group, animals in the SDF/ ***GM*** - ***CSF*** group exhibited increased endothelial progenitor cell density (21.7 +/- 3.2 vs 9.6 +/- 3.1 CD34(+)/vascular endothelial growth factor receptor 2-positive cells per high-power field, P = .01). There was enhanced vascularity (44.1 +/- 5.5 versus 23.8 +/- 2.2 von Willebrand factor-positive vessels per high-power field, P = .007). SDF/ ***GM*** - ***CSF*** group animals experienced less adverse ventricular remodeling, as manifested by less cavity dilatation (9.8 +/- 0.1 mm vs 10.1 +/- 0.1 mm [control], P = .04) and increased border-zone wall thickness (1.78 +/- 0.19 vs 1.41 +/- 0.16 mm [control], P = .03). (SDF/ ***GM*** - ***CSF*** group animals had improved cardiac function compared with animals in the saline control group (maximum pressure: 93.9 +/- 3.2 vs 71.7 +/- 3.1 mm Hg, P < .001; maximum dp/dt: 3513 +/- 303 vs 2602 +/- 201 mm Hg/s, P < .05; cardiac output: 21.3 +/- 2.7 vs 13.3 +/- 1.3 mL/min, P < .01; end-systolic pressure-volume relationship slope: 1.7 +/- 0.4 vs 0.5 +/- 0.2 mm Hg/mL, P < .01). Conclusion: This novel revascularization strategy of ***bone*** ***marrow*** stimulation and intramyocardial delivery of the endothelial progenitor cell chemokine stromal cell-derived factor yielded significantly enhanced ***myocardial*** endothelial progenitor cell density, vasculogenesis, geometric preservation, and contractility in a model of ischemic cardiomyopathy. Copyright .COPYRG. 2005 by The American Association for Thoracic Surgery.

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AN 2005323337 EMBASE <<LOGINID::20070126>>

TI Signaling factors in stem cell-mediated repair of infarcted ***myocardium***

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SO Journal of Molecular and Cellular Cardiology, (2005) Vol. 39, No. 2, pp. 363-376.

Refs: 148

ISSN: 0022-2828 CODEN: JMCDA

PUI S 0022-2828(05)00167-7

CY United Kingdom

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy

018 Cardiovascular Diseases and Cardiovascular Surgery

037 Drug Literature Index

LA English

SL English

ED Entered STN: 18 Aug 2005

Last Updated on STN: 18 Aug 2005

AB ***Myocardial*** infarction leads to scar formation and subsequent reduced cardiac performance. The ultimate therapy after ***myocardial*** infarction would pursue stem cell-based regeneration. The aim of stem cell-mediated cardiac repair embodies restoration of cardiac function by regeneration of healthy ***myocardial*** tissue, which is accomplished by neo- ***angiogenesis*** and cardiogenesis. A major reservoir of adult autologous stem cells distal from the

heart is the ***bone*** ***marrow***. Adequate regulation of signaling between the ***bone*** ***marrow*** and the peripheral circulation and the infarcted ***myocardium*** is important in orchestrating the process of mobilization, homing, incorporation, survival, proliferation and differentiation of stem cells, that leads to ***myocardial*** regeneration. In this review, we discuss key signaling factors, including cytokines, chemokines and growth factors, which are involved in orchestrating the stem cell driven repair process. We focus on signaling factors known for their mobilizing and chemotactic abilities (SDF-1, G-CSF, SCF, IL-8, VEGF), signaling factors that are expressed after ***myocardial*** infarction involved in the patho-physiological healing process (TNF- α , IL-8, IL-10, ***HIF*** -1 α , VEGF, G-CSF) and signaling factors that are involved in cardiogenesis and neo- ***angiogenesis*** (VEGF, EPO, TGF- β , HGF, ***HIF*** -1 α , IL-8). The future therapeutic application and capacity of secreted factors to modulate tissue repair after ***myocardial*** infarction relies on the intrinsic potency of factors and on the optimal localization and timing of a combination of signaling factors to stimulate stem cells in their niche to regenerate the infarcted ***heart***. .COPYRG. 2005 Elsevier Ltd. All rights reserved.

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AN 2005322784 EMBASE <<LOGINID::20070126>>

TI ***Bone*** ***marrow*** cell-seeded biodegradable polymeric scaffold enhances ***angiogenesis*** and improves function of the infarcted ***heart***

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SO Circulation Journal, (2005) Vol. 69, No. 7, pp. 850-857.

Refs: 29

ISSN: 1346-9843 CODEN: CJIOBY

CY Japan

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

025 Hematology

027 Biophysics, Bioengineering and Medical Instrumentation

037 Drug Literature Index

039 Pharmacy

LA English

SL English

ED Entered STN: 18 Aug 2005

Last Updated on STN: 18 Aug 2005

AB Background: The present study examined whether a bioengineered polyglycolic acid cloth (PGAC) impregnated with ***bone*** ***marrow*** cells (BMC) improved the function and ***angiogenesis*** of the infarcted ***heart***. Methods and Results: The coronary artery was ligated in Lewis rats and the infarcted area was covered with a PGAC in group 1 (n=8), with a PGAC containing basic-fibroblast growth factor (b- ***FGF***) in group 2 (n=11) and a PGAC containing b- ***FGF*** and freshly isolated BMC in group 3 (n=10). In addition, BMC derived from transgenic mice expressing green fluorescent protein (GFP)-BMC were seeded into a PGAC, which was sutured over the infarcted area of C57BL/6 mice (n=5). In the rat study, developed and systolic pressures, dp/dt max and dp/dt min) were the highest in group 3, as were the capillary density in the PGAC and infarcted area. In the mouse study, there were few GFP-BMC in the PGAC, but none in the infarcted area. Conclusions: A PGAC with BMC improved cardiac function by inducing ***angiogenesis*** without migration of BMC. Freshly isolated BMC work as ***angiogenic*** inducers and a PGAC is useful as a "drug delivery system".

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AN 2005226075 EMBASE <<LOGINID::20070126>>

TI Molecularly targeted therapy for gastrointestinal cancer.

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CS M.W. Wiedmann, Department of Internal Medicine II, University of Leipzig, Philipp-Rosenthal-Str. 27, 04103 Leipzig, Germany. wiedm@medizin.uni-leipzig.de

SO Current Cancer Drug Targets, (2005) Vol. 5, No. 3, pp. 171-193.

Refs: 102

ISSN: 1568-0096 CODEN: CCOTB

CY Netherlands

DT Journal; General Review

FS 016 Cancer

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 9 Jun 2005

Last Updated on STN: 9 Jun 2005

AB Receptor and non-receptor tyrosine kinases (TKs) have emerged as clinically useful drug target molecules for treating gastrointestinal cancer. Imatinib mesilate (STI-571, Gleevec.RTM.), an inhibitor of bcr-abl TK, which was primarily designed to treat chronic myeloid leukemia is also an inhibitor of c-kit receptor TK, and is currently the drug of choice for the therapy of metastatic gastrointestinal stromal tumors (GISTs), which frequently express constitutively activated forms of the c-kit-receptor. The epidermal growth factor receptor (EGFR), which is

involved in cell proliferation, metastasis and ***angiogenesis***, is another important target. The two main classes of EGFR inhibitors are the TK inhibitors and monoclonal antibodies. Gefitinib (ZD1839, Iressa.RTM.) has been on trial for esophageal and colorectal cancer (CRC) and erlotinib (OSI-774, Tarceva.RTM.) on trial for esophageal, colorectal, hepatocellular, and biliary carcinoma. In addition, erlotinib has been evaluated in a Phase III study for the treatment of pancreatic cancer. Cetuximab (IMC-C225, Erbitux.RTM.), a monoclonal EGFR antibody, has been FDA approved for the therapy of irinotecan resistant colorectal cancer and has been tested for pancreatic cancer. Vascular endothelial growth factor (VEGF) and its receptor (VEGFR) are critical regulators of tumor ***angiogenesis***. Bevacizumab (Avastin.RTM.), a monoclonal antibody against VEGF, was efficient in two randomized clinical trials investigating the treatment of metastatic colorectal cancer. It is also currently investigated for the therapy of pancreatic cancer in combination with gemcitabine. Other promising new drugs currently under preclinical and clinical evaluation, are VEGFR2 inhibitor PTK787/ZK 222584, thalidomide, farnesyl transferase inhibitor R115777 (tipifarnib, Zarnestra.RTM.), matrix metalloproteinase inhibitors, proteasome inhibitor bortezomib (Velcade.RTM.), mammalian target of rapamycin (mTOR) inhibitors, cyclooxygenase-2 (COX-2) inhibitors, platelet derived growth factor receptor (PDGF-R) inhibitors, protein kinase C (PKC) inhibitors, mitogen-activated protein kinase kinase (MEK) 1/2 inhibitors, Rous sarcoma virus transforming oncogene (SRC) kinase inhibitors, histone deacetylase (HDAC) inhibitors, small hypoxia-inducible factor (***HIF***) inhibitors, aurora kinase inhibitors, hedgehog inhibitors, and TGF- β . signalling inhibitors. .COPYRG. 2005 Bentham Science Publishers Ltd.

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AN 200525105 EMBASE <<LOGINID:20070126>>

TI Homing to hypoxia: ***HIF*** -1 as a mediator of progenitor cell recruitment to injured tissue.

AU Ceradini D.J.; Gurtner G.C.

CS Dr. G.C. Gurtner, New York University Medical Center, TH-169, 550 First Ave, New York, NY 10016, United States. geoffrey.gurtner@med.nyu.edu

SO Trends in Cardiovascular Medicine, (2005) Vol. 15, No. 2, pp. 57-63. .

Refs: 55

ISSN: 1050-1738 CODEN: TCMDEQ

PUI S 1050-1738(05)00012-5

CY United States

DT Journal; (Short Survey)

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

021 Developmental Biology and Teratology

LA English

SL English

ED Entered STN: 9 Jun 2005

Last Updated on STN: 9 Jun 2005

AB The identification of ***bone*** -derived endothelial progenitor cells has altered our understanding of new blood vessel growth and tissue regeneration. Previously, new blood vessel growth in the adult was thought to only occur through ***angiogenesis***, the sprouting of new vessels from existing structures. However, it has become clear that circulating ***bone*** -derived cells can form new blood vessels through a process of postnatal vasculogenesis, with endothelial progenitor cells selectively recruited to injured or ischemic tissue. How this process occurs has remained unclear. One common element in the different environments where vasculogenesis is believed to occur is the presence of a hypoxic stimulus. We have identified the chemokine stromal cell-derived factor-1 (SDF-1) and its receptor CXCR4 as critical mediators for the ***ischemia*** -specific recruitment of circulating progenitor cells. We have found that the endothelial expression of SDF-1 acts as a signal indicating the presence of tissue ***ischemia***, and that its expression is directly regulated by hypoxia-inducible factor-1. Stromal cell-derived factor 1 is the only chemokine family member known to be regulated in this manner. Later events, including proliferation, patterning, and assembly of recruited progenitors into functional blood vessels, are also influenced by tissue oxygen tension and hypoxia. Interestingly, both SDF-1 and hypoxia are present in the ***bone*** -***marrow*** niche, suggesting that hypoxia may be a fundamental requirement for progenitor cell trafficking and function. As such, ischemic tissue may represent a conditional stem cell niche, with recruitment and retention of circulating progenitors regulated by hypoxia through differential expression of SDF-1. .COPYRG. 2005, Elsevier Inc.

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AN 2005152592 EMBASE <<LOGINID:20070126>>

TI Impairment in postischemic neovascularization in mice lacking the CXC chemokine receptor 3.

AU Waeckel L.; Mallat Z.; Potteaux S.; Combadiere C.; Clergue M.; Duriez M.; Bao L.; Gerard C.; Rollins B.J.; Tedgui A.; Levy B.I.; Silvestre J.-S.

CS J.-S. Silvestre, U541-INSERM, Hopital Lariboisiere, 41 Bd de la Chapelle, 75475 Paris Cedex 10, France. Jean-Sebastien.Silvestre@larib.inserm.fr

SO Circulation Research, (18 Mar 2005) Vol. 96, No. 5, pp. 576-582. .

Refs: 16

ISSN: 0009-7330 CODEN: CIRUAL

CY United States

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy

018 Cardiovascular Diseases and Cardiovascular Surgery

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 28 Apr 2005

Last Updated on STN: 28 Apr 2005

AB Inflammatory cell infiltration is a feature of postischemic neovascularization. However, mechanisms leading to leukocyte attraction to the site of neovascularization are still undefined. We hypothesized that the CXC chemokine receptor 3 (CXCR3) may contribute to leukocyte accumulation and subsequently to blood vessel growth in the ischemic area. ***ischemia*** induced by femoral artery ligation improved the number of CXCR3-expressing cells and the level of its ligand, CXCL10. Angiographic score, blood flow recovery measurement, and capillary density analysis showed a significant decrease of ischemic/nonischemic leg ratio in CXCR3-deficient mice when compared with controls (P<0.05), at day 21 after ***ischemia***. Interestingly, this impairment was as important as that observed in mice deficient for the well known CC-chemokine monocyte chemoattractant protein-1 (***MCP*** -1). At day 7 of ischemic injury, the number of CD3-positive T cells and Mac-3-positive monocytes/macrophages was 38% and 45% lower, respectively, in the ischemic leg of CXCR3-deficient mice compared with the control group (P<0.05), suggesting an important role for CXCR3 in leukocyte recruitment into the ischemic area. VEGF protein content, a classical proangiogenic factor, was also markedly reduced (80% reduction) in ischemic leg of CXCR3-deficient mice (P<0.01). Injection of ***bone*** -***marrow*** -derived mononuclear cells (BM-MNCs) isolated from wild-type animals restored the neovascularization reaction in CXCR3-deficient mice whereas BM-MNCs from CXCR3-deficient mice was ineffective. In conclusion, CXCR3 plays a key role in neovascularization and provides novel information on the mechanisms leading to leukocyte infiltration in the vessel growth area. .COPYRG. 2005 American ***Heart*** Association, Inc.

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AN 2004382558 EMBASE <<LOGINID:20070126>>

TI Influence of mechanical, cellular, and molecular factors on collateral artery growth (Arteriogenesis).

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CS Dr. W. Schaper, Max-Planck-Inst. Physiol./Clin. Res., Dept. of Experimental Cardiology, Benkestrasse 2, 61231 Bad Nauheim, Germany. w.schaper@kerckhoff.mpg.de

SO Circulation Research, (3 Sep 2004) Vol. 95, No. 5, pp. 449-458. .

Refs: 88

ISSN: 0009-7330 CODEN: CIRUAL

CY United States

DT Journal; General Review

FS 002 Physiology

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 24 Sep 2004

Last Updated on STN: 24 Sep 2004

AB Growth of collateral blood vessels (arteriogenesis) is potentially able to preserve structure and function of limbs and organs after occlusion of a major artery. The success of the remodeling process depends on the following conditions: (1) existence of an arteriolar network that connects the preocclusive with the postocclusive microcirculation; (2) activation of the arteriolar endothelium by elevated fluid shear stress; (3) invasion (but not incorporation) of ***bone*** -***marrow*** -derived cells; and (4) proliferation of endothelial and smooth muscle cells. Most organs of most mammals including man can rely on the existence of interconnecting arterioles in most organs and tissues with ***heart*** being the exception in rodents and pigs. Arterial occlusion lowers the pressure in the distal vasculature thereby creating a pressure gradient favoring increased flow through preexisting collaterals. This increases fluid shear stress leading to endothelial activation with cellular edema, upregulation of adhesion molecules, mitogenic-, thrombogenic-, and fibrinolytic factors, leading to monocyte invasion with matrix digestion. Smooth muscle cells migrate and proliferate and the vessel enlarges under the influence of increasing circumferential wall stress. Growth factors involved belong to the ***FGF*** family and signaling proceeds via the Ras/Raf- and the Rho cascades. Increases in vascular radius and wall thickness restore fluid shear stress and circumferential wall stress to normal levels and growth stops. Although increases in collateral vessel size are very substantial their maximal conductance amounts to only 40% of normal. Forced increases in FSS can reach almost 100%.

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AN 2004230684 EMBASE <<LOGINID:20070126>>

TI Gene transfer of stromal cell-derived factor-1.alpha. enhances ischemic vasculogenesis and ***angiogenesis*** via vascular endothelial growth factor/endothelial nitric oxide synthase-related pathway: Next-generation chemokine therapy for therapeutic neovascularization.

AU Hiasa K.-I.; Ishibashi M.; Ohtani K.; Inoue S.; Zhao Q.; Kitamoto S.; Sata M.; Ichiki T.; Takeshita A.; Egashira K.

CS Dr. K. Egashira, Dept. of Cardiovascular Medicine, Graduate School of Medical Science, Kyushu University, 3-1-1, Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan. egashira@cardiol.med.kyushu-u.ac.jp

SO Circulation, (25 May 2004) Vol. 109, No. 20, pp. 2454-2461. .

Refs: 36

ISSN: 0009-7322 CODEN: CIRCAZ

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
LA English
SL English
ED Entered STN: 28 Jun 2004
Last Updated on STN: 28 Jun 2004

AB Background-Stromal cell-derived factor-1.alpha. (SDF-1.alpha.) is implicated as a chemokine for endothelial progenitor cells (EPCs). We therefore hypothesized that SDF-1.alpha. gene transfer would induce therapeutic neovascularization in vivo by functioning as a chemokine of EPC. Methods and Results-To examine SDF-1.alpha.-induced mobilization of EPC, we used ***bone*** ***marrow*** -transplanted mice whose blood cells ubiquitously express .beta.-galactosidase (LacZ). We produced unilateral hindlimb ***ischemia*** in the mice and transfected them with plasmid DNA encoding SDF-1.alpha. or empty plasmids into the ischemic muscles. SDF-1.alpha. gene transfer mobilized EPCs into the peripheral blood, augmented recovery of blood perfusion to the ischemic ***limb***, and increased capillary density associated with partial incorporation of LacZ-positive cells into the capillaries of the ischemic ***limb***, suggesting that SDF-1.alpha. induced vasculogenesis and ***angiogenesis***. SDF-1.alpha. gene transfer did not affect ***ischemia*** -induced expression of vascular endothelial growth factor (VEGF) but did enhance Akt and endothelial nitric oxide synthase (eNOS) activity. Blockade of VEGF or ***NOS*** prevented all such SDF-1.alpha.-induced effects. Conclusions-SDF-1.alpha. gene transfer enhanced ***ischemia*** -induced vasculogenesis and ***angiogenesis*** in vivo through a VEGF/eNOS-related pathway. This strategy might become a novel chemokine therapy for next generation therapeutic neovascularization.

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AN 2004138324 EMBASE <<LOGINID::20070126>>

TI Marrow-Derived Stromal Cells Express Genes Encoding a Broad Spectrum of Arteriogenic Cytokines and Promote In Vitro and In Vivo Arteriogenesis Through Paracrine Mechanisms.

AU Kinnaird T.; Stabile E.; Burnett M.S.; Lee C.W.; Barr S.; Fuchs S.; Epstein S.E.

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SO Circulation Research, (19 Mar 2004) Vol. 94, No. 5, pp. 678-685. .
Refs: 34

ISSN: 0009-7330 CODEN: CIRUAL

CY United States
DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery
021 Developmental Biology and Teratology
027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry

LA English
SL English

ED Entered STN: 15 Apr 2004

Last Updated on STN: 15 Apr 2004

AB We recently demonstrated that marrow stromal cells (MSCs) augment collateral remodeling through release of several cytokines such as VEGF and bFGF rather than via cell incorporation into new or remodeling vessels. The present study was designed to characterize the full spectrum of cytokine genes expressed by MSCs and to further examine the role of paracrine mechanisms that underpin their therapeutic potential. Normal human MSCs were cultured under normoxic or hypoxic conditions for 72 hours. The gene expression profile of the cells was determined using Affymetrix GeneChips representing 12 000 genes. A wide array of arteriogenic cytokine genes were expressed at baseline, and several were induced > 1.5-fold by hypoxic stress. The gene array data were confirmed using ELISA assays and immunoblotting of the MSC conditioned media (MSC(CM)). MSC(CM) promoted in vitro proliferation and migration of endothelial cells in a dose-dependent manner; anti-VEGF and anti-***FGF*** antibodies only partially attenuated these effects. Similarly, MSC (CM) promoted smooth muscle cell proliferation and migration in a dose-dependent manner. Using a murine hindlimb ***ischemia*** model, murine MSC (CM) enhanced collateral flow recovery and remodeling, improved ***limb*** function, reduced the incidence of autoamputation, and attenuated muscle atrophy compared with control media. These data indicate that paracrine signaling is an important mediator of ***bone*** ***marrow*** cell therapy in tissue ***ischemia***, and that cell incorporation into vessels is not a prerequisite for their effects.

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AN 2004128804 EMBASE <<LOGINID::20070126>>

TI A phase I vaccine safety and chemotherapy dose-finding trial of an allogeneic ***GM*** - ***CSF*** -secreting breast cancer vaccine given in a specifically timed sequence with immunomodulatory doses of cyclophosphamide and doxorubicin.

AU Emens L.A.; Armstrong D.; Biedrzycki B.; Davidson N.; Davis-Sprout J.; Fetting J.; Jaffee E.; Onners B.; Piantadosi S.; Reilly R.T.; Stearns V.; Tartakovsky I.; Visvanathan K.; Wolf A.

CS Dr. L.A. Emens, 1650 Orleans Street, Baltimore, MD 21231-2410, United States. emensle@jhmi.edu

SO Human Gene Therapy, (2004) Vol. 15, No. 3, pp. 313-337. .

Refs: 87

ISSN: 1043-0342 CODEN: HGTHE3

CY United States

DT Journal; General Review

FS 022 Human Genetics

026 Immunology, Serology and Transplantation

037 Drug Literature Index

038 Adverse Reactions Titles

052 Toxicology

LA English

ED Entered STN: 29 Apr 2004

Last Updated on STN: 29 Apr 2004

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

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AN 2003479716 EMBASE <<LOGINID::20070126>>

TI Carcinoid: A Comprehensive Review.

AU Schnirer I.I.; Yao J.C.; Ajani J.A.

CS J.A. Ajani, Department of GI Oncology, Box 78, Univ. TX M. D. Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77005-4341, United States. Jajani@mdanderson.org

SO Acta Oncologica, (2003) Vol. 42, No. 7, pp. 672-692. .

Refs: 248

ISSN: 0284-186X CODEN: ACTOEL

CY Norway

DT Journal; General Review

FS 003 Endocrinology

008 Neurology and Neurosurgery

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 11 Dec 2003

Last Updated on STN: 11 Dec 2003

AB Carcinoid tumors originate from the neuroendocrine cells throughout the body and are capable of producing various peptides. Their clinical course is often indolent but can also be aggressive and resistant to therapy. We examined all aspects of carcinoid tumors including the molecular biology oncogenesis, role of ***angiogenesis***, recent advances in imaging, and therapy. The Medline and Cancerlit databases were searched using carcinoid as the keyword. English language manuscripts were reviewed and relevant references from a total of 7 741 were found. All titles were screened and all the relevant manuscripts were analyzed; we found 307 references pertinent to the history, epidemiology, clinical behavior, pathology, pathophysiology, molecular biology, radiologic imaging, supportive care of carcinoid syndrome, and results of therapeutic clinical trials. Management of patients with carcinoid tumors requires an understanding of the disease process and a multimodality approach. Introduction of long-acting somatostatin analogues has resulted in significant advances in the palliative care of patients with carcinoid syndrome. However, advanced carcinoid tumor remains incurable. Existing therapies for advanced disease have low biologic activity, high toxicity, or both. Clearly, more research is necessary in the areas of molecular biology, targeted therapy, and development of new drugs. Future advances in this field need to focus on clinical and biological predictors of outcome. Early works in the area of tumor biology such as the role of p53, bcl-2, bax, MEN1, ***FGF***, TGF, PDGF and VEGF expression are of interest and need to be explored further.

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AN 2003009122 EMBASE <<LOGINID::20070126>>

TI [Cell transplants and gene therapy. New methods of treatment of post-infarction circulatory insufficiency].

PRZESZCZEPY KOMORKOWE I TERAPIA GENOWA. NOWE METODY LECZENIA POZAWAJOWEJ NIEWYDOLNOSCI KRAZENIA.

AU Rozwadowska N.; Fisz D.; Siminiak T.; Kalawski R.; Kurpisz M.

CS Prof. M. Kurpisz, Zakład Genetyki Człowieka Pan, ul. Strzeszyńska 32, 60-479 Poznań, Poland. kurpimac@man.poznan.pl

SO Polski Przegląd Kardiologiczny, (2002) Vol. 4, No. 4, pp. 325-329. .

Refs: 29

ISSN: 1507-5540 CODEN: PPKOAO

CY Poland

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

022 Human Genetics

037 Drug Literature Index

LA Polish

SL Polish; English

ED Entered STN: 16 Jan 2003

Last Updated on STN: 16 Jan 2003

AB The number of cases of post-infarction circulatory insufficiency is still on rise and presently employed forms of therapy do not directly access to the pathologically malformed tissue. The proposed, new therapeutic attempt is based on cellular engineering and gene therapy or combination of both. So far, there have been proposed autologous ***bone*** ***marrow*** cells, fibroblasts, myoblasts or kardiomyocytes as the source of tissue transplants to the post-infarction scar. Gene therapy is based upon administration of constructs containing genes connected with ***angiogenic*** process: VEGF (vascular endothelial growth factor), bFGF/bFGF2 (basic fibroblast growth factor), PDGF-BB (platelet-derived

growth factor) and ***HIF*** -1 alpha (hypoxia-inducible factor-1 alpha). As well cellular engineering as gene therapy were studied first in animal models. Majority of protocols were successful therefore phase I clinical trials began; at present even phase II clinical trials have been initiated. Collection of the data will allow to optimize a therapy and perhaps will deliver to patients and physicians a long awaited solution, i.e. successful treatment of increasing cases of post-infarction circulatory insufficiency. A present review summarizes new methods of treatment of post-infarcted ***heart***.

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AN 2001164293 EMBASE <<LOGINID:20070126>>

TI Inducible nitric oxide synthase (iNOS) activity promotes ischaemic skin flap survival.

AU Kane A.J.; Barker J.E.; Mitchell G.M.; Theile D.R.B.; Romero R.; Messina A.; Wagh M.; Fraulin F.O.G.; Morrison W.A.; Stewart A.G.

CS A.G. Stewart, Department of Pharmacology, University of Melbourne, Parkville, Vic. 3052, Australia. a.stewart@pharmacology.unimelb.edu.au

SO British Journal of Pharmacology, (2001) Vol. 132, No. 8, pp. 1631-1638. Refs: 34

ISSN: 0007-1188 CODEN: BJPCBM

CY United Kingdom

DT Journal; Article

FS 030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 23 May 2001

Last Updated on STN: 23 May 2001

AB 1. We have examined the role of nitric oxide (NO) in a model of functional ***angiogenesis*** in which survival of a skin flap depends entirely on ***angiogenesis*** to provide an arterial blood supply to maintain tissue viability. 2. The different effects of nitric oxide synthase (***NOS***) inhibitors on rat skin flap survival appeared to be explained on the basis of their ***NOS*** isoform selectivity. Skin flap survival was decreased by iNOS-selective (inducible ***NOS***) inhibitors, S-methyl-isothiourea, aminoguanidine and amino-ethylthiourea; unaffected by the non-selective inhibitor nitro-imino-L-ornithine; and enhanced by the cNOS (constitutive ***NOS*** , that is endothelial ***NOS*** (eNOS) and neuronal ***NOS*** (nNOS)) inhibitor, nitro-L-arginine methyl ester. 3. Skin flap survival was reduced in mice with targeted disruption of the iNOS gene (iNOS knockout mice), and the administration of nitro-L-arginine methyl ester significantly increased flap survival in iNOS knockout mice (P<0.05). 4. iNOS immunoreactivity was identified in mast cells in the ***angiogenic*** region. Immunoreactive vascular endothelial growth factor (VEGF) and basic fibroblast growth factor were also localized to mast cells. 5. The combination of interferon-gamma and tumour necrosis factor-alpha induced NO production and increased VEGF levels in mast cells cultured from ***bone*** ***marrow*** of wild-type, but not iNOS KO mice. 6. The increased tissue survival associated with the capacity for iNOS expression may be related to iNOS-dependent enhancement of VEGF levels and an ensuing ***angiogenic*** response. Our results provide both pharmacological and genetic evidence that iNOS activity promotes survival of ischaemic tissue.

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AN 2001161051 EMBASE <<LOGINID:20070126>>

TI Transendocardial delivery of autologous ***bone*** ***marrow*** enhances collateral perfusion and regional function in pigs with chronic experimental ***myocardial*** ***ischemia***.

AU Fuchs S.; Baffour R.; Yi Fu Zhou; Shou M.; Pierre A.; Tio F.O.; Weissman N.J.; Leon M.B.; Epstein S.E.; Komowski R.

CS Dr. S. Fuchs, Cardiovascular Research Institute, Washington Hospital Center, 110 Irving St. Northwest, Washington, DC 20010, United States. sxf6@mhg.edu

SO Journal of the American College of Cardiology, (2001) Vol. 37, No. 6, pp. 1726-1732. Refs: 33

ISSN: 0735-1097 CODEN: JACCDI

PUI S 0735-1097(01)01200-1

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

LA English

SL English

ED Entered STN: 17 May 2001

Last Updated on STN: 17 May 2001

AB OBJECTIVES: We tested the hypothesis that intramyocardial injection of autologous ***bone*** ***marrow*** (ABM) promotes collateral development in ischemic porcine ***myocardium***. We also defined, in vitro, whether ***bone*** ***marrow*** (BM) cells secrete vascular endothelial growth factor (VEGF) and macrophage chemoattractant protein-1 (***MCP*** - ***1***). BACKGROUND: The natural processes leading to collateral development are extremely complex, requiring multiple growth factors interacting in concert and in sequence. Because optimal ***angiogenesis*** may, therefore, require multiple ***angiogenic*** factors, we thought that injection of BM, which contains cells that secrete numerous ***angiogenic*** factors, might provide optimal therapeutic ***angiogenesis***. METHODS: ***Bone***

marrow was cultured four weeks in vitro. Conditioned medium was assayed for VEGF and ***MCP*** - ***1*** and was added to cultured pig aortic endothelial cells (PAEC) to assess proliferation. Four weeks after left circumflex ameroid implantation, freshly aspirated ABM (n = 7) or heparinized saline (n = 7) was injected transendocardially into the ischemic zone (0.2 ml/injection at 12 sites). Echocardiography to assess ***myocardial*** thickening and microspheres to assess perfusion were performed at rest and during stress. RESULTS: Vascular endothelial growth factor and ***MCP*** - ***1*** concentrations increased in a time-related manner. The conditioned medium enhanced, in a dose-related manner, PAEC proliferation. Collateral flow (ischemic/normal zone x 100) improved in ABM-treated pigs (ABM: 98 +/- 14 vs. 83 +/- 12 at rest; p = 0.001; 89 +/- 18 vs. 78 +/- 12 during adenosine, p = 0.025; controls: 92 +/- 10 vs. 89 +/- 9 at rest, p = 0.49; 78 +/- 11 vs. 77 +/- 5 during adenosine, p = 0.75). Similarly, contractility increased in ABM-treated pigs (ABM: 83 +/- 21 vs. 60 +/- 32 at rest, p = 0.04; 91 +/- 44 vs. 36 +/- 43 during pacing, p = 0.056; controls: 69 +/- 48 vs. 64 +/- 46 at rest, p = 0.74; 65 +/- 56 vs. 37 +/- 56 during pacing, p = 0.23). CONCLUSIONS: ***Bone*** ***marrow*** cells secrete ***angiogenic*** factors that induce endothelial cell proliferation and, when injected transendocardially, augment collateral perfusion and ***myocardial*** function in ischemic ***myocardium***. .COPYRG.T. 2001 by the American College of Cardiology.

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AN 2000358889 EMBASE <<LOGINID:20070126>>

TI [***Angiogenesis*** and vasculogenesis. Therapeutic approaches for stimulation of post-natal neovascularization].

ANGIOGENESE UND VASKULOGENESE THERAPEUTISCHE

STRATEGIEN ZUR

STIMULATION DER POSTNATALEN NEOVASKULARISATION.

AU Kalka C.; Asahara T.; Krone W.; Isner J.M.

CS Dr. C. Kalka, Cardiovascular Research, St. Elizabeth's Medical Center, 736 Cambridge Street, Boston, MA 02135, United States. Ckalka@juno.com

SO Herz, (2000) Vol. 25, No. 6, pp. 611-622. Refs: 91

ISSN: 0340-9937 CODEN: HERZDW

CY Germany

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

030 Pharmacology

037 Drug Literature Index

LA German

SL English; German

ED Entered STN: 2 Nov 2000

Last Updated on STN: 2 Nov 2000

AB The ***formation*** of new ***blood*** ***vessel*** is essential for a variety of physiological processes like embryogenesis and the female reproduction as well as wound healing and neovascularization of ischemic tissue. Major progress in understanding the underlying mechanisms regulating blood vessel growth has offered novel therapeutic options in the treatment of a variety of diseases including ischemic cardiovascular disorders. Vasculogenesis and ***angiogenesis*** are the mechanisms responsible for the development of the blood vessels. ***Angiogenesis*** refers to the formation of capillaries from preexisting vessels in the embryo and adult organism. While pathologic ***angiogenesis*** includes the role of post-natal neovascularization in the pathogenesis of arthritis, diabetic retinopathy, and tumor growth and metastasis, therapeutic ***angiogenesis***, either endogenously or in response to administered growth factors, includes the development of collateral blood vessels in tissue ***ischemia***. Preclinical studies established that ***angiogenic*** growth factors could promote collateral artery development in animal models of peripheral and ***myocardial*** ***ischemia***. Subsequent clinical trials using gene transfer of naked DNA encoding for VEGF for the treatment of critical ***limb*** and ***myocardial*** ***ischemia*** documented the safety and clinical benefit of this novel therapeutic approach. Several objective methods indicated marked improvement in collateral vessel development. Vasculogenesis describes the development of new blood vessels from in situ differentiating endothelial cells. Recently considered to be restricted to embryogenesis, there exists now striking evidence that endothelial progenitor cells (EPC) circulate also in adult peripheral blood able to participate in ongoing neovascularization. Different cytokines and growth factors have a stimulatory effect on these ***bone*** - ***marrow*** derived EPC. Granulocyte macrophage colony stimulating factor (***GM*** - ***CSF***) and vascular endothelial growth factor (VEGF) mobilize EPC from the ***bone*** ***marrow*** into the peripheral circulation. While their endogenous contribution to postnatal neovascularization needs to be documented, the iatrogenic expansion and mobilization of EPC might represent an effective means to augment the resident population of endothelial cells (ECs). This kind of cell therapy for tissue regeneration in ischemic cardiovascular diseases opens a novel and challenging clinical option besides or in addition to the use of growth factors in gene therapy.

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AN 1999137095 EMBASE <<LOGINID:20070126>>

TI ***Ischemia*** - and cytokine-induced mobilization of ***bone***

marrow -derived endothelial progenitor cells for neovascularization.

AU Takahashi T.; Kalka C.; Masuda H.; Chen D.; Silver M.; Kearney M.; Magner

M.; Isner J.M.; Asahara T.
CS J.M. Isner, Department of Medicine, St. Elizabeth's Medical Center, Tufts University School of Medicine, 736 Cambridge Street, Boston, MA 02135-2997, United States

SO Nature Medicine, (1999) Vol. 5, No. 4, pp. 434-438.
Refs: 18

ISSN: 1078-8956 CODEN: NAMEFI

CY United States

DT Journal; Article

FS 006 Internal Medicine

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 12 May 1999

Last Updated on STN: 12 May 1999

AB Endothelial progenitor cells (EPCs) have been isolated from circulating mononuclear cells in human peripheral blood and shown to be incorporated into foci of neovascularization, consistent with postnatal vasculogenesis. We determined whether endogenous stimuli (tissue ***ischemia***) and exogenous cytokine therapy (granulocyte macrophage-colony stimulating factor, ***GM*** - ***CSF***) mobilize EPCs and thereby contribute to neovascularization of ischemic tissues. The development of regional ***ischemia*** in both mice and rabbits increased the frequency of circulating EPCs. In mice, the effect of ***ischemia*** - induced EPC mobilization was demonstrated by enhanced ocular neovascularization after cornea micropocket surgery in mice with hindlimb ***ischemia*** compared with that in non-ischemic control mice. In rabbits with hindlimb ***ischemia*** , circulating EPCs were further augmented after pretreatment with ***GM*** - ***CSF*** , with a corresponding improvement in hindlimb neovascularization. There was direct evidence that EPCs that contributed to enhanced corneal neovascularization were specifically mobilized from the ***bone*** ***marrow*** in response to ***ischemia*** and ***GM*** - ***CSF*** in mice transplanted with ***bone*** ***marrow*** from transgenic donors expressing beta-galactosidase transcriptionally regulated by the endothelial cell-specific Tie-2 promoter. These findings indicate that circulating EPCs are mobilized endogenously in response to tissue ***ischemia*** or exogenously by cytokine therapy and thereby augment neovascularization of ischemic tissues.

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AN 2007:52013 BIOSIS <<LOGINID::20070126>>

DN PREV200700052829

TI ***Bone*** ***marrow*** may be a useful therapy in osteomyelitis.

AU Namazi, Hamid [Reprint Author]

CS Shiraz Univ, Iran Shiraz Chamran Hosp, Shiraz, Iran

namazih@sums.ac.ir

SO Medical Hypotheses, (2006) Vol. 67, No. 6, pp. 1464.

CODEN: MEHYDY. ISSN: 0306-9877.

DT Letter

Editorial

LA English

ED Entered STN: 10 Jan 2007

Last Updated on STN: 10 Jan 2007

=> FIL STNGUIDE

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AN 2007:52013 BIOSIS <<LOGINID::20070126>>

DN PREV200700052829

TI ***Bone*** ***marrow*** may be a useful therapy in osteomyelitis.

AU Namazi, Hamid [Reprint Author]

CS Shiraz Univ, Iran Shiraz Chamran Hosp, Shiraz, Iran

namazih@sums.ac.ir

SO Medical Hypotheses, (2006) Vol. 67, No. 6, pp. 1464.

CODEN: MEHYDY. ISSN: 0306-9877.

DT Letter

Editorial

LA English

ED Entered STN: 10 Jan 2007

Last Updated on STN: 10 Jan 2007

L15 ANSWER 21 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2007:48149 BIOSIS <<LOGINID::20070126>>

DN PREV200700049010

TI Combined cytokine therapy (G-CSF and ***GM*** - ***CSF***) in acute

myocardial infarction stimulates monocyte-derived pro-

angiogenic cells and improves ***myocardial*** perfusion.

AU Scacciatella, P. [Reprint Author]; Bruno, S.; Usmani, T.; D'amico, M.;
Andriani, M.; Camussi, G.; Tarella, C.; Marra, S.

CS Azienda Osped SG Battista, Turin, Italy

SO European Heart Journal, (AUG 2006) Vol. 27, No. Suppl. 1, pp. 279.

Meeting Info.: World Congress of Cardiology. Barcelona, SPAIN. September
02 -06, 2006.

CODEN: EHJODF. ISSN: 0195-668X.

DT Conference; (Meeting)

Conference; (Meeting Poster)

LA English

ED Entered STN: 10 Jan 2007

Last Updated on STN: 10 Jan 2007

L15 ANSWER 22 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:530561 BIOSIS <<LOGINID::20070126>>

DN PREV200600529370

TI ACE inhibitor raps CD26/dipeptidylpeptidase IV knuckles for cytokine EPC
mobilization.

AU Asahara, Takayuki [Reprint Author]

CS Tokai Univ, Sch Med, Dept Regenerat Med Sci, Tokai, Ibaraki, Japan

asa777@aol.com

SO Journal of Molecular and Cellular Cardiology, (JUL 2006) Vol. 41, No. 1,
pp. 8-10.

CODEN: JMCDAJ. ISSN: 0022-2828.

DT Article

Editorial

LA English

ED Entered STN: 12 Oct 2006

Last Updated on STN: 12 Oct 2006

L15 ANSWER 23 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:522619 BIOSIS <<LOGINID::20070126>>

DN PREV200600523749

TI Synthetic vascular prosthesis impregnated with mesenchymal stem cells
overexpressing endothelial nitric oxide synthase.

AU Kanki-Horimoto, Sachiko [Reprint Author]; Horimoto, Hitoshi; Mieno,
Shigetoshi; Kishida, Kenji; Watanabe, Fusao; Furuya, Eisuke; Katsumata,
Takashi

CS Osaka Med Coll, Dept Thorac and Cardiovasc Surg, 2-7 Daigakumachi
Takatsuki, Osaka 5698686, Japan

tho064@poh.osaka-med.ac.jp

SO Circulation, (JUL 4 2006) Vol. 114, No. Suppl. 1, pp. I327-I330.

CODEN: CIRCZJ. ISSN: 0009-7322.

DT Article

Editorial

LA English

ED Entered STN: 12 Oct 2006

Last Updated on STN: 12 Oct 2006

AB Background-Endothelial dysfunction is known to exaggerate coronary artery
disease, sometimes leading to irreversible ***myocardial*** damage.
In such cases, repetitive coronary revascularization including coronary
artery bypass grafting is needed, which may cause a shortage of graft
conduits. On the other hand, endothelial nitric oxide synthase (eNOS) is
an attractive target of cardiovascular gene therapy. The vascular
prostheses, of which the inner surfaces are covered with mesenchymal stem
cells (MSCs) overexpressing eNOS, are expected to offer feasible effects
of NO and ***angiogenic*** effects of MSCs on the native coronary
arterial beds, as well as improvement of self-patency. Herein, we

attempted to develop small caliber vascular prostheses generating the bioactive proteins. Also, we attempted to transduce eNOS cDNA into MSCs. Methods and Results-The MSCs were isolated from rat ***bone*** marrow*** and transduced with each adenovirus harboring rat eNOS cDNA and beta-galactosidase (beta-gal) (eNOS/MSCs and beta-gal/ MSCs). The beta-gal/MSCs were impregnated into vascular prostheses, then the expressions of beta-gal on the inner surfaces of them were evaluated by 5-bromo-4-chloro-3-indolyl beta-D-galactoside staining. The ***NOS*** activity of eNOS/MSCs was assayed by monitoring the conversion of H-3-arginine to H-3-citrulline. The inner surfaces of the vascular prostheses were covered with MSCs expressing beta-gal. The amount of the H-3-citrulline increased, and eNOS/MSCs were determined to generate enzymatic activity of eNOS. This activity was completely inhibited by N-G-nitro-L-arginine methyl ester. Conclusions-The inner surface of expanded polytetrafluoroethylene vascular prostheses seeded with lacZ gene-transduced MSCs exhibited recombinant proteins. Development of eNOS/MSC-seeded vascular prostheses would promise much longer graft patency and vasculoprotective effects.

L15 ANSWER 24 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:467485 BIOSIS <<LOGINID::20070126>>

DN PREV200600465279

TI Therapeutic ***angiogenesis*** - Another passing phase?.

AU Semenza, Gregg L. [Reprint Author]

CS Johns Hopkins Univ, Sch Med, Vasc Biol Program, Inst Cell Engr, Dept Pediat, Broadway Res Bldg, Suite 671, 733 N Broadway, Baltimore, MD 21205 USA
gsemenza@jhmi.edu

SO Circulation Research, (MAY 12 2006) Vol. 98, No. 9, pp. 1115-1116.

CODEN: CIRUAL. ISSN: 0009-7330.

DT Article

Editorial

LA English

ED Entered STN: 20 Sep 2006

Last Updated on STN: 20 Sep 2006

L15 ANSWER 25 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:459458 BIOSIS <<LOGINID::20070126>>

DN PREV200600449865

TI Small molecule approaches for promoting ischemic tissue vascularization.

AU Bussolino, Federico [Reprint Author]

CS Inst Canc Res and Treatment, Dept Oncol Sci, Div Mol Angiogenesis, Str Provinciale 142, I-10060 Turin, Italy
federico.bussolino@irc.it

SO Circulation Research, (AUG 4 2006) Vol. 99, No. 3, pp. 231-233.

CODEN: CIRUAL. ISSN: 0009-7330.

DT Article

LA English

ED Entered STN: 13 Sep 2006

Last Updated on STN: 13 Sep 2006

L15 ANSWER 26 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:182922 BIOSIS <<LOGINID::20070126>>

DN PREV200600185034

TI Purified peritoneal macrophages do not promote ***angiogenesis*** in vivo.

AU Pelletier, Patricia [Reprint Author]; Perri, Sabrina; Francois, Moira; Copland, Ian; Galipeau, Jacques

CS McGill Univ, Lady Davis Inst Med Res, Dept Med, Montreal, PQ, Canada
SO Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 748A.

Meeting Info: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA, December 10-13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 15 Mar 2006

Last Updated on STN: 15 Mar 2006

AB A large number of patients suffer from peripheral vascular disease not amenable to surgery, thus making medical therapies that promote neovascularization, including cell-based therapies, of interest. It is known that macrophages play an important role in ***angiogenesis*** in the context of wound healing and tumors, and that ***bone*** marrow*** (BM)-derived and peripheral blood (PB) mononuclear cells injected in ischemic limbs of animal models can favor development of collateral vessels. In order to determine the specific contribution of monocytes/macrophages to ***angiogenesis*** in an in vivo mouse model, we studied new vessel formation in a subcutaneously implanted Matrigel matrix plug in which peritoneal macrophages were embedded. We also tested whether macrophage exposure to ***GM*** - ***CSF*** would enhance their pro- ***angiogenic*** effect. A cohort of C57B1/6 mice was sacrificed 6 days after intraperitoneal injection of 10% thioglycollate. Stimulated peritoneal macrophages were collected and plated in RPMI 1640 supplemented with 10% FBS (R10). Adherent macrophages were trypsinized, resuspended in 500 μ L of Matrigel, and injected subcutaneously in C57B1/6 mice. The 4 experimental groups consisted of: Matrigel alone (n=5), with 5.7x10(6) macrophages (n=4), with murine ***GM*** -

CSF 500u/mL (n=5), and with both 5.7x10(6) macrophages and murine

GM - ***CSF*** 500u/mL (n=6). Matrigel plugs were resected at 21 days and endothelial cells on histological sections were stained with anti-WVF antibody. For each implant, blood vessels were counted on one

entire section, excluding the periphery. The mean number of blood vessels per mm(2) (+/- SEM) was: Matrigel alone: 4.0 (+/- 1.4), Matrigel +

GM - ***CSF*** : 2.6 (+/- 1.1), Matrigel + macrophages: 5.3 (+/- 1.2), Matrigel + GMCSF + macrophages: 4.7 (+/- 0.9). There was no statistically significant difference in new vessel formation among the four groups (p > 0.1 by Student T test). In a separate experiment,

adherent peritoneal macrophages were cultured in R10 with or without ***GM*** - ***CSF*** 500u/mL for 24 hours. The cells were then washed

thoroughly and cultured in serum-free Opti media for 18 hours. A RayBiotech antibody array testing 24 pro- and anti- ***angiogenic***

cytokines was performed using concentrated conditioned media. It demonstrated that peritoneal macrophages secrete a number of pro-

angiogenic /arteriogenic cytokines such as ***MCP*** - ***VEGF***, bFGF and ***GM*** - ***CSF***, as well as anti-

angiogenic cytokines such as TIMP-1 and IL-12. However, the cytokine profile was not significantly altered by stimulation of cells with ***GM*** - ***CSF***. In summary, a purified population of

peritoneal macrophages failed to significantly alter host-derived ***angiogenesis*** in a Matrigel subcutaneous implant, despite the

detectable presence of pro- ***angiogenic*** cytokines. This may be explained in part by the concomitant secretion of anti- ***angiogenic***

factors. Some clinical trials have successfully achieved ***angiogenesis*** in cardiovascular disease using unfractionated

BM-derived or PB mononuclear cells. Considering that the proportion of monocytes in these preparations by far outnumbered that of stem and

progenitor cells with hemangioblast potential, it might be worthwhile exploring whether removing monocytes from unfractionated mononuclear cell

collections would promote a distinct and possibly enhanced proangiogenic effect.[GRAPHICS]

L15 ANSWER 27 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:182573 BIOSIS <<LOGINID::20070126>>

DN PREV200600184685

TI Hypoxia-inducible factor 1 mediated expression of hypoxia-induced vascular endothelial growth factor in human ***bone*** ***marrow*** stromal cells, which is involved in MAP kinase and phosphatidylinositol 3-kinase signaling.

AU Tang, Guangxiao [Reprint Author]; Liu, Gexiu

CS Jinan Univ, Med Coll, Inst Hematol, Guangzhou, Peoples R China

SO Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 651A-652A.

Meeting Info: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA, December 10-13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

LA English

ED Entered STN: 15 Mar 2006

Last Updated on STN: 15 Mar 2006

AB INTRODUCTION: Recent studies indicate that transplantation of ***bone***

marrow stromal cells after rat traumatic brain injury provided functional recovery. Hypoxia is the major characteristic of ischemic

microenvironment. Vascular endothelial growth factor (VEGF) has been demonstrated in vivo and in vitro to be the principal mediator of

hypoxia-induced ***angiogenesis***. Recent studies indicate that VEGF implicated in neuroprotection. We tested the hypothesis that hypoxia

induces expression of vascular endothelial growth factor (VEGF) in human ***bone*** ***marrow*** stromal cells (hBMSC) by hypoxia-inducible

factor 1 (***HIF*** -1). METHODS: Human ***bone*** ***marrow*** adherent cells were cultured, and were passaged in DMEM/F12 containing 10% FBS. The fifth passage cells were identified as stromal cells.

Subconfluent cells were used, and were cultured with hypoxic DMEM/F12 in hypoxia condition (94% N-2 + 1% O-2 +5% CO2), and were treated with 50 μ M PD98059, or 200 nM wortmannin, or siRNA specific for ***HIF*** -1

mRNA. Cells were harvested after 6 h for analysis of active phosphorylated kinases (Akt and MAPK) and the ***HIF*** -1-alpha

protein or after 24 h for analysis of VEGF protein and mRNA. VEGF mRNA was detected by semi-quantitative RT-PCR, and VEGF protein by ELISA, and kinases and the ***HIF*** -1-alpha protein by Western blot. RESULTS:

Hypoxia increased significantly level of both VEGF mRNA and VEGF protein in hBMSC s, which were low level in normoxic cultured cells. 24 hours

after treatment, ratio of RT-PCR product between VEGF and beta-actin reach to (46.25 +/- 7.54)% from (19.61 +/- 4.57)% of control cells (P < 0.01).

VEGF protein increased to (142.77 +/- 22.33) pg/ml from (45.85 +/- 9.69) pg/ml (P < 0.01). In addition, hypoxia induced active phosphorylated

kinases (Akt and MAPK), and enhanced level of the ***HIF*** -1-alpha protein. Moreover, PD98059, or wortmannin, or siRNA specific for the

HIF -1-alpha mRNA inhibited induction of the VEGF gene by hypoxia. CONCLUSION: The expression of VEGF mRNA and VEGF increased

in human

bone ***marrow*** stromal cells during hypoxia condition, which is involved in MAP kinase and phosphatidylinositol 3-kinase

signaling. These results support that these cells play an important role in therapy of ischemic/hypoxic injury such as cerebral ***ischemia***

and ***myocardial*** ***ischemia***. The hBMSC capacity to increase expression of VEGF maybe the key to the benefit provided by

transplanted hBMSCs in the ischemic injuries.

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AN 2006:86053 BIOSIS <<LOGINID::20070126>>

DN PREV200600081646

TI Tissue-resident ***bone*** ***marrow*** -derived progenitor cells - Key players in hypoxia-induced ***angiogenesis***

AU Garin, Gwenaelle; Mathews, Marlene; Berk, Bradford C. [Reprint Author]

CS Univ Rochester, Dept Med, Med Ctr, Box MED, Rochester, NY 14642 USA
bradford_berk@urmc.rochester.edu

SO Circulation Research, (NOV 11 2005) Vol. 97, No. 10, pp. 955-957.
CODEN: CIRUAL. ISSN: 0009-7330.

DT Article

Editorial

LA English

ED Entered STN: 25 Jan 2006

Last Updated on STN: 25 Jan 2006

L15 ANSWER 29 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2005:536008 BIOSIS <<LOGINID::20070126>>

DN PREV200510321511

TI Endothelial nitric oxide synthase (eNOS) gene-transfected vascular prosthesis with ***bone*** ***marrow*** cell transplantation.

AU Horimoto, Sachiko [Reprint Author]; Mieno, Shigetoshi; Horimoto, Hitoshi; Kishida, Kenji; Watanabe, Fusao; Furuya, Eisuke; Katsumata, Takahiro

CS Osaka Med Coll, Dept Thorac and Cardiovasc Surg, Osaka 5698686, Japan

SO FASEB Journal, (MAR 7 2005) Vol. 19, No. 5, Suppl. S, Part 2, pp. A1677.

Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci.
CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 Dec 2005

Last Updated on STN: 1 Dec 2005

AB Introduction; Therapeutic ***angiogenesis*** by ***bone***

marrow cell (BMC) transplantation has been clinically available for the treatment of ischemic cardiovascular disease. Endothelial nitric oxide synthase (eNOS) is an attractive target of cardiovascular gene therapy to elicit ***angiogenic***, cytoprotective and vasculoprotective effects. Herein, we attempted to develop vascular prosthesis (VP) generating enzymatic activity of eNOS by using gene-engineering. Method: The replication-deficient adenovirus was constructed harboring rat eNOS cDNA and beta galactosidase (beta gal) cDNA under the control of the cytomegalovirus promoter. The BMCs were isolated from six-week male SD rats and transfected with each adenovirus (eNOS/BMC, beta gal/BMC, respectively). The beta gal/BMC was impregnated into VP, then the expressions of beta gal was evaluated by X-gal stain. The ***eNOS*** activity of eNOS/BMC was assayed by monitoring the conversion of H-3-arginine to 3 H-citrulline. Result: The luminal surface of the VP was covered with BMC expressing beta gal. The amount of the H-3-citrulline was increased and eNOS/BMC was determined to generate enzymatic activity of eNOS. Conclusion: These data suggest that eNOS/BMC preserves valid biochemical property of eNOS, implicating that eNOS gene-transfected VP can exert enzymatic activity of eNOS. Results of the present study may lead to development of a novel clinical relevant VP.

L15 ANSWER 30 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2005:524816 BIOSIS <<LOGINID::20070126>>

DN PREV200510314779

TI Granulocyte colony-stimulating factor (G-CSF) is synthesized and released from the ***heart*** in the early phase of acute ***myocardial*** infarction.

AU Fujiwara, Takayuki [Reprint Author]; Kameda, Kunihiko; Abe, Naoki; Matsunaga, Toshiro; Okumura, Ken

CS Hirosaki Univ, Sch Med, Hirosaki, Aomori 036, Japan

SO Circulation, (OCT 26 2004) Vol. 110, No. 17, Suppl. S, pp. 250.

Meeting Info.: 77th Scientific Meeting of the American Heart Association. New Orleans, LA, USA, November 07 -10, 2004. Amer Heart Assoc.
CODEN: CIRCAZ. ISSN: 0009-7322.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 Dec 2005

Last Updated on STN: 1 Dec 2005

AB Granulocyte colony-stimulating factor (G-CSF) is a hematopoietic growth factor that regulates the production and differentiation of neutrophils.

Recently, G-CSF has been reported to mobilize ***bone*** ***marrow*** stem cells, which may differentiate into cardiac myocytes after acute ***myocardial*** infarction (AMI). However, the plasma level of G-CSF level and its regulation in patients with ischemic ***heart*** disease (IHD) remain unclear. Several ***angiogenic*** growth factors were reported to be accumulated at high concentrations in the pericardial fluid (PF) in patients with IHD. We measured G-CSF, vascular endothelial growth factor (VEGF) and granulocyte-macrophage colony-stimulating factor (***GM*** - ***CSF***) levels in the PF

obtained from 72 patients with IHD who underwent coronary artery bypass graft surgery (CABG) using specific enzyme immunoassay (EIA) kits. Among 72 patients, 20 had AMI and other 52 angina pectoris (AP). All patients with AMI underwent emergency CABG within 24 hours after the onset of AMI. G-CSF level in PF was markedly increased in patients with AMI (57.4 +/- 48.5 pg/ml) compared with patients with AP (4.6 +/- 2.4 pg/ml, p<0.0001). There was no difference in the PF levels of VEGF (490 +/- 100 vs 426 +/- 66 pg/ml) and ***GM*** - ***CSF*** (0.21 +/- 0.23 vs 0.29 +/- 0.35 pg/ml) between AMI and AP groups. In another group of 18 patients with AMI, we collected blood samples from the coronary sinus (CS) and aorta during primary coronary angioplasty done within 12 hours after the onset of AMI, and measured the plasma G-CSF level. The plasma G-CSF level was higher in CS than in the aorta (8.5 +/- 2.1 vs 7.0 +/- 1.8 pg/ml, p<0.05). The G-CSF level in the aorta in AMI patients was not different from that in the venous blood in AP patients (6.6 +/- 1.3 pg/ml). These plasma G-CSF levels, however, were significantly higher than that in normal subjects (3.7 +/- 1.4 pg/ml, n=5, p<0.05 vs AMI and AP). In conclusion, G-CSF is synthesized and released from cardiac tissue in the early phase of AMI. This cardiac tissue-derived G-CSF may play an important role for the recruitment of stem/progenitor cells and the regeneration of cardiomyocytes after AMI.

L15 ANSWER 31 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2005:347886 BIOSIS <<LOGINID::20070126>>

DN PREV200510144036

TI Upregulating the expression of ***angiogenesis*** -related genes by transplanting autologous mononuclear ***bone*** ***marrow*** cells into ***myocardial*** infarction scar and the periphery.

AU Sun Yong-xin; Zhao Qiang [Reprint Author]; Wang Yi-qing; Yang Cheng; Pan Cui-zhen; Han Pei-pei; Chen Rui-zhen; Yang Ying-zhen; Wang Ke-qiang; Ge Jun-bo

CS Fudan Univ, Zhongshan Hosp, Shanghai Inst Cardiovasc Dis, Dept Cardiovasc

Surg, Shanghai 200032, Peoples R China

SO Zhonghua Xinxueguanbing Zazhi, (MAR 19 2005) Vol. 33, No. 3, pp. 260-264.
CODEN: CHHCDF. ISSN: 0253-3758.

DT Article

LA Chinese

ED Entered STN: 8 Sep 2005

Last Updated on STN: 8 Sep 2005

AB Objective To detect the regulation of ***angiogenic*** genes involved in the processes of collateral development. Methods ***Myocardial*** infarction (MI) scar was induced by cryoinjury in New Zealand rabbits. Four weeks after MI, 24 hours before cell transplantation, ***bone*** ***marrow*** was aspirated from the right high bone and mononuclear ***bone*** ***marrow*** cells (BMCs) were isolated by Ficoll density gradient centrifugation. Then the mononuclear BMCs (n = 8) or IMDM culture medium (n = 8) were transplanted into infarction scar and the periphery. Four weeks after mononuclear BMCs transplantation, DNA microarray analysis was performed to detect the regulation of ***angiogenesis*** -related genes in infarction scar and the periphery. And the differences of ***angiogenic*** genes expression were compared among several important growth factors by Western blot. Results DNA microarray analysis showed the detail regulation of genes involved in the ***angiogenic*** processes. There were 15 genes upregulated over 3 times in the infarction scar. In addition, we also found more genes are involved in the process of ***angiogenesis*** in its periphery than in the infarction scar (40 genes vs. 15 genes). Western blot analysis further demonstrated that mononuclear BMCs transplantation was capable of increasing the levels of VEGF, ***FGF*** and Angiopoietin-I expression in the infarction scar and its periphery, compared with the control group, P < 0.05. Conclusion These findings indicate that the natural ***angiogenic*** processes leading to collateral development are extremely complex, since many kinds of ***bone*** ***marrow*** -derived growth factors involved in the processes after mononuclear BMCs transplantation into infarction sites.

L15 ANSWER 32 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2004:181009 BIOSIS <<LOGINID::20070126>>

DN PREV200400181001

TI Granulocyte Colony-Stimulating Factor (G-CSF) contributes to mobilization of ***bone*** ***marrow*** -derived endothelial progenitor cells for ischemic neovascularization.

AU Ohki, Yuichi [Reprint Author]; Heissig, Beate; Satoh, Yayoi [Reprint Author]; Shibata, Miki; Shimada, Kazunori [Reprint Author]; Ohsaka, Akimichi; Daida, Hiroyuki [Reprint Author]; Hattori, Koichi

CS Department of Cardiology Medicine, Juntendo University School of Medicine, Tokyo, Japan

SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 39a. print.

Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA, December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 7 Apr 2004

Last Updated on STN: 7 Apr 2004

AB Recent studies indicated that Granulocyte Colony-Stimulating Factor (G-CSF) promotes tumor growth by stimulating ***angiogenesis***. We

hypothesized that G-CSF through mobilization of ***bone*** marrow*** -derived endothelial progenitor cells (EPCs) contributes to neovascularization of ischemic tissue. Freshly isolated peripheral blood mononuclear cells (PBMCs) obtained from BALB/C mice treated with G-CSF (4mg/body) were cultured in endothelial growth medium in vitro. Colony forming unit-endothelial cells (CFU-EC) showed LDL uptake (Dil-acetylated-LDL+) and stained positive for Flk-1+CD45- by immunohistochemistry. Neovascularization was assayed using a matrigel assay system in vivo. Mice were injected subcutaneously with Matrigel with/without G-CSF. Matrigel containing VEGF plus ***FGF*** served as positive controls. Vessel formation was observed in G-CSF containing matrigel in the presence or absence of VEGF plus ***FGF***. Similarly, G-CSF stimulated PBMC (5X10⁵ cells/ml matrigel) formed vessels in matrigel containing VEGF/bFGF, whereas unstimulated (G-CSF-treated) PBMC in VEGF/bFGF containing matrigel failed to form any vessels. These data implicate that G-CSF promotes neovascularisation by mobilizing immature progenitor cells which in an ***angiogenic*** environment differentiate in mature endothelial cells. On the other hand, G-CSF can directly mobilize immature endothelial progenitors ready to incorporate into ischemic tissue. We finally asked whether local administration of G-CSF into ischemic tissue using a murine hind- ***limb*** model - tissue known to provide an ***angiogenic*** environment - will promote revascularisation. We injected G-CSF intra-muscular (do-4) into the ischemic hind- ***limb*** muscle. Local administration of G-CSF 21 days after treatment resulting in increased capillary density in the G-CSF group as compared to controls. These findings indicate that G-CSF therapy promotes vasculogenesis by promoting the mobilization of ***bone*** marrow*** -derived EPCs into circulation. On the other hand, local administration of G-CSF may increase the number of immature cells, which set into an ***angiogenic*** environment are able to differentiate into the endothelial cell lineage and provide functionally active vasculature. These data provide evidence that local administration of G-CSF into ischemic tissue may provide a novel and safe therapeutic strategy to improve neovascularization.

L15 ANSWER 33 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

AN 2004:154892 BIOSIS <<LOGINID::20070126>>

DN PREV200400148414

TI Spred-1 negatively regulates cytokine-induced MAP kinase activation in hematopoietic cells.

AU Nonami, Atsushi [Reprint Author]; Kato, Reiko [Reprint Author]; Harada, Mine; Yoshimura, Akihiko [Reprint Author]

CS Molecular and Cellular Immunology, Medical Institute of Bioregulation of Kyushu University, Fukuoka, Japan

SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 833a, print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA, December 06-09, 2003. American Society of Hematology. CODEN: BLOOD. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Mar 2004

Last Updated on STN: 17 Mar 2004

AB Receptor tyrosine kinases (RTKs), such as stem cell factor (SCF) receptor c-kit, and cytokine receptors, such as interleukin (IL)-3 or erythropoietin (EPO) receptor, activate the MAP kinase/ERK (extracellular signal-regulated kinases) cascade. MAP kinases play an important role in hematopoiesis. Most hematopoietic cytokines activate the JAK-STAT and Ras-ERK pathways, both of which are required for sufficient proliferation and differentiation of hematopoietic cells. MAP kinases also play a critical role in megakaryopoiesis induced by c-mpl. However, little is known regarding the regulation of MAP kinase in hematopoietic cells. Recently, we cloned a family of novel membrane bound molecules, Spreds, which are c-kit binding proteins related to Sprouty. Drosophila Sprouty was identified as a negative regulator of ERK activation induced by several growth factors, including ***FGF*** and EGF. Four Sprouty homologues have been identified in mammals. Vertebrate Sproutys have been implicated in negative-feedback regulation of ***FGF*** -signaling in embryogenesis and ***angiogenesis***, although their mechanism of inhibition remains controversial. We have identified three Spred family proteins in mammals, which have a Sprouty-related C-terminal cysteine rich (SPR) domain, in addition to an N-terminal Ena/VASP homology (EVH) 1 domain. The SPR-domain of Sprouty, and probably Spred, is palmitoylated, causing localization to the membrane fraction. Like Sprouty, Spred-1, Spred-2, and Spred-3 also downregulate Ras/ERK signaling. We have shown that Spred interacts with ras and inhibits Raf kinase activation without reducing Ras activation, and interestingly, it also stabilizes EGF-induced Raf-1 translocation from the cytosol to the plasma membrane. As Spred inhibits Ras-induced ERK activation, it might modulate unidentified steps of Raf activation by a novel mechanism. Moreover, a C-terminal deletion mutant of Spred-1 functions as a dominant negative and augments serum and NGF-induced ERK activation. The physiological function of Spred/Sprouty family proteins remains to be investigated. Spred-1 expression was reported to be high in the brain and ***heart***, and we found that it is also highly expressed in hematopoietic cells. To investigate the role of Spred-1 in hematopoietic cells, we expressed Spred-1 in IL-3- and SCF-dependent cell lines as well as hematopoietic progenitor cells from mouse ***bone*** marrow*** using retroviral gene transfer. In IL-3 dependent Ba/F3 cells expressing c-kit, forced expression of Spred-1 reduced the proliferation rate and decreased ERK activation in response to

IL-3 and SCF. SCF-dependent cell migration was also suppressed by wild-type Spred-1 overexpression. In contrast, a dominant negative form of Spred-1, dC-Spred, augmented proliferation and cell migration. Furthermore, wild-type Spred-1 strongly inhibited colony formation in ***bone*** marrow*** cells from mice, whereas dC-Spred enhanced colony formation. These data suggest that Spred-1 acts as a negative regulator of hematopoiesis by regulating hematopoietic growth factor-induced MAP kinase activation in mice. The finding of a negative regulator of cytokine-induced ERK activation facilitates the study of ERK function in hematopoiesis and may be useful for in vitro manipulation of hematopoietic progenitor cell expansion.

L15 ANSWER 34 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

AN 2003:356825 BIOSIS <<LOGINID::20070126>>

DN PREV200300356825

TI Comparison of Umbilical Cord Blood Versus ***Bone*** ***Marrow*** -Derived Endothelial Precursor Cells in Mediating Neovascularization in a NOD/SCID Hind ***Limb*** Injury Model.

AU Finney, M. [Reprint Author]; Martin, J. [Reprint Author]; Swan, J. [Reprint Author]; Kaderet, S. [Reprint Author]; Kozik, M. [Reprint Author]; Emancipator, S. [Reprint Author]; Pompili, V. [Reprint Author]; Haynesworth, S. [Reprint Author]; Fu, P. [Reprint Author]; Laughlin, M. J. [Reprint Author]

CS Medicine, Case Western Reserve University, Cleveland, OH, USA

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2691, print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA, December 06-10, 2002. American Society of Hematology.

CODEN: BLOOD. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Aug 2003

Last Updated on STN: 6 Aug 2003

AB It has been reported that endothelial precursor cells (EPCs) for potential use in therapeutic ***angiogenesis*** can be derived from either umbilical cord blood (UCB) or adult ***bone*** marrow*** (BM). We compared both stem cell sources of EPC in a hind- ***limb*** ***ischemia*** model in the NOD/SCID mouse. Density gradient centrifugation was used to isolate mononuclear cells (MNC) from fresh UCB or BM. Cells were plated on fibronectin coated tissue culture flasks at a density of 4-6 x 10⁶ cells/ml (UCB MNC) or 1-2 x 10⁶ cells/ml (BM MNC) in EBM2 medium (Clonetics) with 5% FBS and standard SingleQuot additives that included VEGF, ***FGF***, IGF, hydrocortisone, ascorbic acid, heparin (Kalka et al. (2000) PNAS 97:3422-3427). Non-adherent cells were removed after 4 days of culture and medium was changed every fourth day thereafter. During the second week of culture, cells adopted the spindle-like morphology characteristic for EPCs. At Day 6-7 cells were trypsinized and counted. Adherent cell yield from UCB cultures were on average 2.5% of initial MNC input, compared to 21.5% obtained from BM MNC. Endothelial characteristics were verified in both cultures by uptake of DiI-labeled acetylated low density lipoprotein and adherence of FITC-conjugated Ulex Europarus lectin visualized by fluorescent microscopy and positive CD31 staining characterized by flow cytometry. Next, 1 x 10⁶ cells were injected into hind- ***limb*** injured mice. For this, a sub-lethal dose of irradiation was given to athymic NOD/SCID mice, and the right femoral artery of each mouse was isolated, ligated and transected at the inguinal ligament level. Immediately after surgery and injection of cells, baseline blood flow of both the ischemic right leg and the non-operated left leg was measured using a laser Doppler flowmeter. Study mice were injected with EPC cells derived from either UCB or BM. Control mice were injected with saline or complete EBM2 medium. Laser Doppler measurements of both hind limbs were taken on days 7, 14 and 28 and tissue samples from lower calf muscle were harvested at day 28 for histological studies. A ratio of perfusion in the ischemic/healthy ***limb*** was used to compare neovascularization in the three study groups. Immediately following femoral ligation the perfusion ratios were 0.057 +/- 0.011 (control group), 0.029 +/- 0.007 (UCB-derived EPC) and 0.018 +/- 0.012 (BM-derived EPC) showing reduced perfusion in all groups. After 14 days, there was a statistically significant difference between groups receiving EPCs compared to the control group. Perfusion ratios in the control group remained low, with 0.24 +/- 0.032 (n=14) compared to 0.41 +/- 0.031 (n=22) in the mouse group receiving UCB-derived EPC (p=0.0008) and 0.42 +/- 0.063 (n=7) in the mouse group receiving BM-derived EPC (p=0.0086). Importantly, there was no significant difference between the two sources of EPCs (p=0.8317). However, after 28 days perfusion ratios of mice that received BM-derived EPCs dropped below control mice while perfusion ratios of mice that received UCB-derived EPCs remained higher than control mice. This observation did not attain statistical significance. Taken together, these results point to possible differences in characteristics of EPC derived from UCB vs BM sources.

L15 ANSWER 35 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

AN 2003:356472 BIOSIS <<LOGINID::20070126>>

DN PREV200300356472

TI Role of ENOS and INOS in Hemangioblast Activity and ***Blood*** ***Vessel*** ***Formation***

AU Guthrie, Steven M. [Reprint Author]; Brown, Gary A. J. [Reprint Author];

Caballero, Sergio [Reprint Author]; Grant, Maria B. [Reprint Author];
 Scott, Edward W. [Reprint Author]
 CS Program in Stem Cell Biology, University of Florida, Gainesville, FL, USA
 SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 458. print.
 Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
 Philadelphia, PA, USA, December 06-10, 2002. American Society of
 Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DT Conference; (Meeting)
 Conference; (Meeting Poster)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 6 Aug 2003
 Last Updated on STN: 18 Sep 2003
 AB Endothelial and Inducible Nitric Oxide Synthases (ENOS/INOS) perform in
 many physiological processes including wound healing, increasing vascular
 permeability, decreasing blood pressure, and vessel remodeling. Recently
 our lab has shown that adult hematopoietic stem cell (HSC) can provide
 functional hemangioblast activity. We hypothesize that ENOS and INOS play
 an important role in new ***blood*** ***vessel***
 formation and hemangioblast activity. ENOS and INOS knock-out
 animals were transplanted with highly purified (c-kit+, sca-1+) green
 fluorescent protein (gfp) ***bone*** ***marrow***. After
 multilineage reconstitution was established rAAV-VEGF was administered and
 one month later retinal ***ischemia*** was induced. The resulting
 neovascularization was quantitated via serial section staining,
 immunohistochemistry, and confocal microscopy. The two isoforms of the
 NOS enzymes have diametrically opposite effects on the type and
 amount of neovascularization. The INOS deficiency yielded vessels which
 were gfp positive indicating that the transplanted HSC contributed to the
 vessel formation. These vessels were highly branched and were shown to be
 functional when the circulatory system was perfused with a fluorescent
 dye. In contrast, ENOS deficiency produced only very large non-branched
 gfp blood vessels, which could not be perfused. The untreated eye of the
 ENOS knockout animal also exhibited the same architecture indicating that
 additional injury is not necessary due to the constant turnover of vessels
 in these animals. These results suggest that alteration in ***NOS***
 activity or NO levels can be used to control the size and branching of new
 vessels formed by the hemangioblast. We are currently testing the effects
 of pharmacologic agents affecting ***NOS*** /NO on hemangioblast
 activity.

L15 ANSWER 36 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson
 Corporation on
 STN
 AN 2003:79552 BIOSIS <<LOGINID::20070126>>
 DN PREV200300079552
 TI Stimulation of nicotinic acetylcholine receptors promotes proliferation,
 activation and homing of endothelial progenitor cells during
 ischemia
 AU Heesch, Christopher [Reprint Author]; Johnson, Frances L.;
 Pathak-Gulati, Anjali; Cooke, John P.
 CS Frankfurt Univ, Frankfurt, Germany
 SO Circulation, (November 5 2002) Vol. 106, No. 19 Supplement, pp. II-64.
 print.
 Meeting Info.: Abstracts from Scientific Sessions. Chicago, IL, USA.
 November 17-20, 2002. American Heart Association.
 ISSN: 0009-7322 (ISSN print).
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 6 Feb 2003
 Last Updated on STN: 6 Feb 2003

L15 ANSWER 37 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson
 Corporation on
 STN
 AN 2001:264108 BIOSIS <<LOGINID::20070126>>
 DN PREV200100264108
 TI The effect of transendocardial delivery of autologous ***bone***
 marrow stimulated by Granulocyte Monocyte Colony Stimulating
 Factor (***GM-CSF***) on ischemic ***myocardial***
 perfusion and function.
 AU Fuchs, Shmuel [Reprint author]; Baffour, Richard [Reprint author]; Shou,
 Matie [Reprint author]; Zhou, Yi Fu [Reprint author]; Tio, Fermin O.
 [Reprint author]; Leon, Martin B. [Reprint author]; Epstein, Stephen E.
 [Reprint author]; Kornowski, Ran [Reprint author]
 CS Cardiovascular Research Institute, Washington Hospital Center, Washington,
 DC, USA
 SO Journal of the American College of Cardiology, (February, 2001) Vol. 37,
 No. 2 Supplement A, pp. 246A. print.
 Meeting Info.: 50th Annual Scientific Session of the American College of
 Cardiology. Orlando, Florida, USA. March 18-21, 2001. American College of
 Cardiology.
 CODEN: JACCDI. ISSN: 0735-1097.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 30 May 2001
 Last Updated on STN: 19 Feb 2002

L15 ANSWER 38 OF 99 BIOSIS COPYRIGHT (c) 2007 The Thomson
 Corporation on

STN
 AN 2000:530295 BIOSIS <<LOGINID::20070126>>
 DN PREV200000530295
 TI Transendocardial delivery of autologous ***bone*** ***marrow***
 enhances collateral perfusion and regional function in pigs with chronic
 experimental ***myocardial*** ***ischemia***
 AU Kornowski, R. [Reprint author]; Fuchs, S. [Reprint author]; Baffour, R.
 [Reprint author]; Shou, M. [Reprint author]; Leon, M. B.; Epstein, S. E.
 [Reprint author]
 CS Cardiovascular Research Institute, Washington Hospital Center, Washington,
 DC, USA
 SO European Heart Journal, (August-September, 2000) Vol. 21, No. Abstract
 Supplement, pp. 356. print.
 Meeting Info.: XXII Congress of the European Society of Cardiology.
 Amsterdam, Netherlands. August 26-30, 2000. European Society of
 Cardiology.
 CODEN: EHJODF. ISSN: 0195-668X.
 DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LA English
 ED Entered STN: 6 Dec 2000
 Last Updated on STN: 11 Jan 2002

L15 ANSWER 39 OF 99 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:1309937 CAPLUS <<LOGINID::20070126>>
 DN 146:55526
 TI Method of treating or preventing pathologic effects of acute increases in
 hyperglycemia and/or acute increases of free fatty acid flux
 IN Gurtner, Geoffrey C.; Brownlee, Michael A.
 PA USA
 SO U.S. Pat. Appl. Publ., 56pp., Cont.-in-part of U.S. Ser. No. 136,254.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006281748	A1	20061214	US 2005-297808	20051207
US 2006100189	A1	20060511	US 2005-136254	20050524
PRAI US 2004-573947P	P	20040524		
US 2005-136254	A2	20050524		

 AB One aspect of the present invention relates to a method of treating or
 preventing pathol. effects of hyperglycemia and/or increased fatty acid
 flux in a subject in need of such treatment or preventive therapy. This
 method involves administering a compn. contg. a therapeutically effective
 amt. of a ROS inhibitor to a subject in need thereof. Deferoxamine
 treatment of diabetic mice exposed to graded ***ischemia*** resulted
 in normalization of wound healing and correction of the diabetes-induced
 defect in ***angiogenesis***

L15 ANSWER 40 OF 99 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:1206177 CAPLUS <<LOGINID::20070126>>
 DN 145:500333
 TI Treatment for ***heart*** disease using a combination of pro-
 angiogenesis therapy and cellular cardiomyoplasty
 IN Dinsmore, Jonathan H.; Jacoby, Douglas B.
 PA Mytogen, Inc., USA
 SO PCT Int. Appl., 115pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006121532	A2	20061116	WO 2006-US12245	20060331

 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
 MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
 SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
 VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 PRAI US 2005-666932P P 20050331
 AB The present invention provides a system for treating ***heart***
 disease using a combination of pro- ***angiogenesis*** therapy and
 cellular cardiomyoplasty. The system is particularly useful in treating
 patients with damaged ***myocardium*** due coronary artery disease,
 myocardial infarction, congestive ***heart*** failure, and
 ischemia. A pro- ***angiogenic*** factor (e.g., VEGF) or a
 means of delivering a pro- ***angiogenic*** factor (e.g., a genetically
 engineered adenovirus, adeno-assocd. virus, or cells) is administered to
 the ***heart*** in order to promote new blood vessel growth in an
 ischemic or damaged area of the patient's ***heart***. Cells such as
 skeletal myoblasts or stem cells (e.g., mesenchymal stem cells) with the
 potential to divide, differentiate, and integrate themselves into the
 injured ***myocardium*** are then administered into the affected area
 of the ***heart***. By inducing new blood vessels growth in the
 injured ***myocardium***, the cells are better able to grow and become

an integral part of the ***heart***. The invention also provides kits for use in treating a patient using the inventive method. Such kits may contain cells, catheters, syringes, needles, cell culture materials, polynucleotides, media, buffers, etc.

=> d his

(FILE 'HOME' ENTERED AT 16:47:24 ON 26 JAN 2007)

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 16:53:37 ON 26 JAN 2007

L1 369490 S BONE MARROW
L2 12787 S L1 AND (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR EPAS1 OR M
L3 26915 S ADENOVIR? (3A) VECTOR
L4 54 S L2 AND L3
L5 50 DUP REM L4 (4 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:04:32 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:23:19 ON 26 JAN 2007

L6 951 S VECTOR (7A) (HIF OR ENDOTHELIAL PAS DOMAIN PROTEIN 1 OR EPAS1
L7 39 S L1 AND L6
L8 26 DUP REM L7 (13 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:33:18 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:39:31 ON 26 JAN 2007

L9 119582 S ANGIOGEN? OR (BLOOD VESSEL (3A) FORM?)
L10 4578 S L1 AND L9
L11 374 S L2 AND L10
L12 374 S L2 AND L9
L13 292 DUP REM L12 (82 DUPLICATES REMOVED)
L14 136 S L13 AND PY<=2003

FILE 'STNGUIDE' ENTERED AT 17:46:26 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 17:51:06 ON 26 JAN 2007

L15 99 S L13 AND (HEART OR MYOCARD? OR LIMB OR ISCHEMIA)

FILE 'STNGUIDE' ENTERED AT 18:01:53 ON 26 JAN 2007

FILE 'EMBASE, BIOSIS, CAPLUS' ENTERED AT 18:15:58 ON 26 JAN 2007

=> dup rem l15

PROCESSING COMPLETED FOR L15

L16 99 DUP REM L15 (0 DUPLICATES REMOVED)

=> s l15 and PY<=2003

L17 27 L15 AND PY<=2003

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 27 ANSWERS - CONTINUE? Y(N):y

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AN 2003479716 EMBASE <<LOGINID:20070126>>

TI Carcinoid: A Comprehensive Review.

AU Schnirer J.I.; Yao J.C.; Ajani J.A.

CS J.A. Ajani, Department of GI Oncology, Box 78, Univ. TX M. D. Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77005-4341, United States. Jajani@mdanderson.org

SO Acta Oncologica, (2003) Vol. 42, No. 7, pp. 672-692.

Refs: 248

ISSN: 0284-186X CODEN: ACTOEL

CY Norway

DT Journal; General Review

FS 003 Endocrinology

008 Neurology and Neurosurgery

016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 11 Dec 2003

Last Updated on STN: 11 Dec 2003

AB Carcinoid tumors originate from the neuroendocrine cells throughout the body and are capable of producing various peptides. Their clinical course is often indolent but can also be aggressive and resistant to therapy. We examined all aspects of carcinoid tumors including the molecular biology oncogenesis, role of ***angiogenesis***, recent advances in imaging, and therapy. The Medline and Cancerlit databases were searched using carcinoid as the keyword. English language manuscripts were reviewed and relevant references from a total of 7 741 were found. All titles were screened and all the relevant manuscripts were analyzed; we found 307 references pertinent to the history, epidemiology, clinical behavior, pathology, pathophysiology, molecular biology, radiologic imaging, supportive care of carcinoid syndrome, and results of therapeutic clinical trials. Management of patients with carcinoid tumors requires an understanding of the disease process and a multimodality approach. Introduction of long-acting somatostatin analogues has resulted in significant advances in the palliative care of patients with carcinoid

syndrome. However, advanced carcinoid tumor remains incurable. Existing therapies for advanced disease have low biologic activity, high toxicity, or both. Clearly, more research is necessary in the areas of molecular biology, targeted therapy, and development of new drugs. Future advances in this field need to focus on clinical and biological predictors of outcome. Early works in the area of tumor biology such as the role of p53, bcl-2, bax, MEN1, ***FGF***, TGF, PDGF and VEGF expression are of interest and need to be explored further.

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AN 2003009122 EMBASE <<LOGINID:20070126>>

TI [Cell transplants and gene therapy. New methods of treatment of post-infarction circulatory insufficiency].

PRZESZCZEPY KOMORKOWE I TERAPIA GENOWA. NOWE METODY

LECZENIA POZAWAIOWEJ

NIWYDOLNOSCI KRAZENIA.

AU Rozwadowska N.; Fiszor D.; Siminiak T.; Kalawski R.; Kurpisz M.

CS Prof. M. Kurpisz, Zakład Genetyki Człowieka Pan, ul. Strzeszyńska 32, 60-479 Poznań, Poland. kurpimac@man.poznan.pl

SO Polski Przegląd Kardiologiczny, (2002) Vol. 4, No. 4, pp. 325-329.

Refs: 29

ISSN: 1507-5540 CODEN: PPKOAO

CY Poland

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

022 Human Genetics

037 Drug Literature Index

LA Polish

SL Polish; English

ED Entered STN: 16 Jan 2003

Last Updated on STN: 16 Jan 2003

AB The number of cases of post-infarction circulatory insufficiency is still on rise and presently employed forms of therapy do not directly access to the pathologically malformed tissue. The proposed, new therapeutic attempt is based on cellular engineering and gene therapy or combination of both. So far, there have been proposed autologous ***bone*** marrow cells, fibroblasts, myoblasts or cardiomyocytes as the source of tissue transplants to the post-infarction scar. Gene therapy is based upon administration of constructs containing genes connected with ***angiogenic*** process: VEGF (vascular endothelial growth factor), bFGF/FGF2 (basic fibroblast growth factor), PDGF-BB (platelet-derived growth factor) and ***HIF*** -1 alpha (hypoxia-inducible factor-1 alpha). As well cellular engineering as gene therapy were studied first in animal models. Majority of protocols were successful therefore phase I clinical trials began; at present even phase II clinical trials have been initiated. Collection of the data will allow to optimize a therapy and perhaps will deliver to patients and physicians a long awaited solution, i.e. successful treatment of increasing cases of post-infarction circulatory insufficiency. A present review summarizes new methods of treatment of post-infarction ***heart***.

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AN 2001164293 EMBASE <<LOGINID:20070126>>

TI Inducible nitric oxide synthase (iNOS) activity promotes ischaemic skin flap survival.

AU Kane A.J.; Barker J.E.; Mitchell G.M.; Theille D.R.B.; Romero R.; Messina A.; Wagh M.; Fraulin F.O.G.; Morrison W.A.; Stewart A.G.

CS A.G. Stewart, Department of Pharmacology, University of Melbourne, Parkville, Vic. 3052, Australia. a.stewart@pharmacology.unimelb.edu.au

SO British Journal of Pharmacology, (2001) Vol. 132, No. 8, pp. 1631-1638.

Refs: 34

ISSN: 0007-1188 CODEN: BJPCBM

CY United Kingdom

DT Journal; Article

FS 030 Pharmacology

037 Drug Literature Index

LA English

SL English

ED Entered STN: 23 May 2001

Last Updated on STN: 23 May 2001

AB 1. We have examined the role of nitric oxide (NO) in a model of functional ***angiogenesis*** in which survival of a skin flap depends entirely on ***angiogenesis*** to provide an arterial blood supply to maintain tissue viability. 2. The different effects of nitric oxide synthase (***NOS***) inhibitors on rat skin flap survival appeared to be explained on the basis of their ***NOS*** isoform selectivity. Skin flap survival was decreased by iNOS-selective (inducible ***NOS***) inhibitors, S-methyl-isothiourea, aminoguanidine and amino-ethylthiourea; unaffected by the non-selective inhibitor nitro-imino-L-ornithine; and enhanced by the cNOS (constitutive ***NOS*** , that is endothelial ***NOS*** (eNOS) and neuronal ***NOS*** (nNOS)) inhibitor, nitro-L-arginine methyl ester. 3. Skin flap survival was reduced in mice with targeted disruption of the iNOS gene (iNOS knockout mice), and the administration of nitro-L-arginine methyl ester significantly increased flap survival in iNOS knockout mice (P<0.05). 4. iNOS immunoreactivity was identified in mast cells in the ***angiogenic*** region. Immunoreactive vascular endothelial growth factor (VEGF) and basic fibroblast growth factor were also localized to mast cells. 5. The combination of interferon-gamma and tumour necrosis factor-alpha, induced NO production and increased VEGF levels in mast cells cultured from ***bone*** marrow of wild-type, but not iNOS KO mice.

6. The increased tissue survival associated with the capacity for iNOS expression may be related to iNOS-dependent enhancement of VEGF levels and an ensuing ***angiogenic*** response. Our results provide both pharmacological and genetic evidence that iNOS actively promotes survival of ischaemic tissue.

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AN 2001161051 EMBASE <<LOGINID:20070126>>

TI Transendocardial delivery of autologous ***bone*** ***marrow*** enhances collateral perfusion and regional function in pigs with chronic experimental ***myocardial*** ***ischemia***.

AU Fuchs S.; Baffour R.; Yi Fu Zhou; Shou M.; Pierre A.; Tio F.O.; Weissman N.J.; Leon M.B.; Epstein S.E.; Komowski R.

CS Dr. S. Fuchs, Cardiovascular Research Institute, Washington Hospital Center, 110 Irving St. Northwest, Washington, DC 20010, United States. sx66@mhg.edu

SO Journal of the American College of Cardiology, (2001) Vol. 37, No. 6, pp. 1726-1732.

Refs: 33

ISSN: 0735-1097 CODEN: JACCDI

PUI S 0735-1097(01)01200-1

CY United States

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

LA English

SL English

ED Entered STN: 17 May 2001

Last Updated on STN: 17 May 2001

AB OBJECTIVES: We tested the hypothesis that intramyocardial injection of autologous ***bone*** ***marrow*** (ABM) promotes collateral development in ischemic porcine ***myocardium***. We also defined, in vitro, whether ***bone*** ***marrow*** (BM) cells secrete vascular endothelial growth factor (VEGF) and macrophage chemoattractant protein-1 (***MCP*** - ***1***). BACKGROUND: The natural processes leading to collateral development are extremely complex, requiring multiple growth factors interacting in concert and in sequence. Because optimal ***angiogenesis*** may, therefore, require multiple ***angiogenic*** factors, we thought that injection of BM, which contains cells that secrete numerous ***angiogenic*** factors, might provide optimal therapeutic ***angiogenesis***. METHODS: ***Bone*** ***marrow*** was cultured four weeks in vitro. Conditioned medium was assayed for VEGF and ***MCP*** - ***1*** and was added to cultured pig aortic endothelial cells (PAEC) to assess proliferation. Four weeks after left circumflex ameroid implantation, freshly aspirated ABM (n = 7) or heparinized saline (n = 7) was injected transendocardially into the ischemic zone (0.2 ml/injection at 12 sites). Echocardiography to assess ***myocardial*** thickening and microsphere to assess perfusion were performed at rest and during stress. RESULTS: Vascular endothelial growth factor and ***MCP*** - ***1*** concentrations increased in a time-related manner. The conditioned medium enhanced, in a dose-related manner, PAEC proliferation. Collateral flow (ischemic/normal zone x 100) improved in ABM-treated pigs (ABM: 98 +/- 14 vs. 83 +/- 12 at rest, p = 0.001; 89 +/- 18 vs. 78 +/- 12 during adenosine, p = 0.025; controls: 92 +/- 10 vs. 89 +/- 9 at rest, p = 0.49; 78 +/- 11 vs. 77 +/- 5 during adenosine, p = 0.75). Similarly, contractility increased in ABM-treated pigs (ABM: 83 +/- 21 vs. 60 +/- 32 at rest, p = 0.04; 91 +/- 44 vs. 36 +/- 43 during pacing, p = 0.056; controls: 69 +/- 48 vs. 64 +/- 46 at rest, p = 0.74; 65 +/- 56 vs. 37 +/- 56 during pacing, p = 0.23). CONCLUSIONS: ***Bone*** ***marrow*** cells secrete ***angiogenic*** factors that induce endothelial cell proliferation and, when injected transendocardially, augment collateral perfusion and ***myocardial*** function in ischemic ***myocardium***. COPYRIGHT. 2001 by the American College of Cardiology.

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AN 200035889 EMBASE <<LOGINID:20070126>>

TI [***Angiogenesis*** and vasculogenesis. Therapeutic approaches for stimulation of post-natal neovascularization].

ANGIOGENESE UND VASKULOGENESE THERAPEUTISCHE

STRATEGIEN ZUR STIMULATION DER POSTNATALEN NEOVASKULARISATION.

AU Kalka C.; Asahara T.; Krone W.; Isner J.M.

CS Dr. C. Kalka, Cardiovascular Research, St. Elizabeth's Medical Center, 736 Cambridge Street, Boston, MA 02135, United States. Ckalka@juno.com

SO Herz, (2000) Vol. 25, No. 6, pp. 611-622.

Refs: 91

ISSN: 0340-9937 CODEN: HERZDW

CY Germany

DT Journal; Article

FS 018 Cardiovascular Diseases and Cardiovascular Surgery

030 Pharmacology

037 Drug Literature Index

LA German

SL English; German

ED Entered STN: 2 Nov 2000

Last Updated on STN: 2 Nov 2000

AB The ***formation*** of new ***blood*** ***vessel*** is essential for a variety of physiological processes like embryogenesis and the female reproduction as well as wound healing and neovascularization of ischemic tissue. Major progress in understanding the underlying

mechanisms regulating blood vessel growth has offered novel therapeutic options in the treatment of a variety of diseases including ischemic cardiovascular disorders. Vasculogenesis and ***angiogenesis*** are the mechanisms responsible for the development of the blood vessels.

Angiogenesis refers to the formation of capillaries from preexisting vessels in the embryo and adult organism. While pathologic ***angiogenesis*** includes the role of post-natal neovascularization in the pathogenesis of arthritis, diabetic retinopathy, and tumor growth and metastasis, therapeutic ***angiogenesis***, either endogenously or in response to administered growth factors, includes the development of collateral blood vessels in tissue ***ischemia***. Preclinical studies established that ***angiogenic*** growth factors could promote collateral artery development in animal models of peripheral and ***myocardial*** ***ischemia***. Subsequent clinical trials using gene transfer of naked DNA encoding for VEGF for the treatment of critical ***limb*** and ***myocardial*** ***ischemia*** documented the safety and clinical benefit of this novel therapeutic approach. Several objective methods indicated marked improvement in collateral vessel development. Vasculogenesis describes the development of new blood vessels from in situ differentiating endothelial cells. Recently considered to be restricted to embryogenesis, there exists now striking evidence that endothelial progenitor cells (EPC) circulate also in adult peripheral blood able to participate in ongoing neovascularization. Different cytokines and growth factors have a stimulatory effect on these ***bone*** - ***marrow*** derived EPC. Granulocyte macrophage colony stimulating factor (***GM*** - ***CSF***) and vascular endothelial growth factor (VEGF) mobilize EPC from the ***bone*** ***marrow*** into the peripheral circulation. While their endogenous contribution to postnatal neovascularization needs to be documented, the iatrogenic expansion and mobilization of EPC might represent an effective means to augment the resident population of endothelial cells (ECs). This kind of cell therapy for tissue regeneration in ischemic cardiovascular diseases opens a novel and challenging clinical option besides or in addition to the use of growth factors in gene therapy.

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AN 1999137095 EMBASE <<LOGINID:20070126>>

TI ***Ischemia*** - and cytokine-induced mobilization of ***bone*** ***marrow*** -derived endothelial progenitor cells for neovascularization.

AU Takahashi T.; Kalka C.; Masuda H.; Chen D.; Silver M.; Kearney M.; Magner M.; Isner J.M.; Asahara T.

CS J.M. Isner, Department of Medicine, St. Elizabeth's Medical Center, Tufts University School of Medicine, 736 Cambridge Street, Boston, MA 02135-2997, United States

SO Nature Medicine, (1999) Vol. 5, No. 4, pp. 434-438.

Refs: 18

ISSN: 1078-8956 CODEN: NAMEFI

CY United States

DT Journal; Article

FS 006 Internal Medicine

029 Clinical Biochemistry

LA English

SL English

ED Entered STN: 12 May 1999

Last Updated on STN: 12 May 1999

AB Endothelial progenitor cells (EPCs) have been isolated from circulating mononuclear cells in human peripheral blood and shown to be incorporated into foci of neovascularization, consistent with postnatal vasculogenesis. We determined whether endogenous stimuli (tissue ***ischemia***) and exogenous cytokine therapy (granulocyte macrophage-colony stimulating factor, ***GM*** - ***CSF***) mobilize EPCs and thereby contribute to neovascularization of ischemic tissues. The development of regional ***ischemia*** in both mice and rabbits increased the frequency of circulating EPCs. In mice, the effect of ***ischemia*** - induced EPC mobilization was demonstrated by enhanced ocular neovascularization after cornea micropocket surgery in mice with hindlimb ***ischemia*** compared with that in non-ischemic control mice. In rabbits with hindlimb ***ischemia***, circulating EPCs were further augmented after pretreatment with ***GM*** - ***CSF***, with a corresponding improvement in hindlimb neovascularization. There was direct evidence that EPCs that contributed to enhanced corneal neovascularization were specifically mobilized from the ***bone*** ***marrow*** in response to ***ischemia*** and ***GM*** - ***CSF*** in mice transplanted with ***bone*** ***marrow*** from transgenic donors expressing beta-galactosidase transcriptionally regulated by the endothelial cell-specific Tie-2 promoter. These findings indicate that circulating EPCs are mobilized endogenously in response to tissue ***ischemia*** or exogenously by cytokine therapy and thereby augment neovascularization of ischemic tissues.

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AN 2004:181009 BIOSIS <<LOGINID:20070126>>

DN PREV200400181001

TI Granulocyte Colony-Stimulating Factor (G-CSF) contributes to mobilization of ***bone*** ***marrow*** -derived endothelial progenitor cells for ischemic neovascularization.

AU Ohki, Yuichi [Reprint Author]; Heissig, Beate; Satoh, Yayoi [Reprint Author]; Shibata, Miki; Shimada, Kazunori [Reprint Author]; Ohsaka, Akimichi; Daida, Hiroyuki [Reprint Author]; Hattori, Koichi

CS Department of Cardiology Medicine, Juntendo University School of Medicine,

Tokyo, Japan
SO Blood, (***November 16 2003***) Vol. 102, No. 11, pp. 39a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.
San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 7 Apr 2004

Last Updated on STN: 7 Apr 2004

AB Recent studies indicated that Granulocyte Colony-Stimulating Factor (G-CSF) promotes tumor growth by stimulating ***angiogenesis***. We hypothesized that G-CSF through mobilization of ***bone***-derived endothelial progenitor cells (EPCs) contributes to neovascularization of ischemic tissue. Freshly isolated peripheral blood mononuclear cells (PBMCs) obtained from BALB/C mice treated with G-CSF (4mg/body) were cultured in endothelial growth medium in vitro. Colony forming unit-endothelial cells (CFU-EC) showed LDL uptake (DiI-acetylated-LDL+) and stained positive for Flk-1+CD45- by immunohistochemistry. Neovascularization was assayed using a matrigel assay system in vivo. Mice were injected subcutaneously with Matrigel with/without G-CSF. Matrigel containing VEGF plus ***FGF*** served as positive controls. Vessel formation was observed in G-CSF containing matrigel in the presence or absence of VEGF plus ***FGF***. Similarly, G-CSF stimulated PBMC (5X10⁵ cells/ml matrigel) formed vessels in matrigel containing VEGF/bFGF, whereas unstimulated (G-CSF-treated) PBMC in VEGF/bFGF containing matrigel failed to form any vessels. These data implicate that G-CSF promotes neovascularization by mobilizing immature progenitor cells which in an ***angiogenic*** environment differentiate in mature endothelial cells. On the other hand, G-CSF can directly mobilize immature endothelial progenitors ready to incorporate into ischemic tissue. We finally asked whether local administration of G-CSF into ischemic tissue using a murine hind- ***limb*** model - tissue known to provide an ***angiogenic*** environment - will promote revascularization. We injected G-CSF intra-muscular (do-d4) into the ischemic hind- ***limb*** muscle. Local administration of G-CSF 21 days after treatment resulting in increased capillary density in the G-CSF group as compared to controls. These findings indicate that G-CSF therapy promotes vasculogenesis by promoting the mobilization of ***bone***-derived EPCs into circulation. On the other hand, local administration of G-CSF may increase the number of immature cells, which set into an ***angiogenic*** environment are able to differentiate into the endothelial cell lineage and provide functionally active vasculature. These data provide evidence that local administration of G-CSF into ischemic tissue may provide a novel and save therapeutic strategy to improve neovascularization.

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AN 2004:154892 BIOSIS <<LOGINID::20070126>>

DN PREV200400148414

TI Spred-1 negatively regulates cytokine-induced MAP kinase activation in hematopoietic cells.

AU Nonami, Atsushi [Reprint Author]; Kato, Reiko [Reprint Author]; Harada, Mine; Yoshimura, Akihiko [Reprint Author]

CS Molecular and Cellular Immunology, Medical Institute of Bioregulation of Kyushu University, Fukuoka, Japan

SO Blood, (***November 16 2003***) Vol. 102, No. 11, pp. 833a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.
San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Mar 2004

Last Updated on STN: 17 Mar 2004

AB Receptor tyrosine kinases (RTKs), such as stem cell factor (SCF) receptor c-kit, and cytokine receptors, such as interleukin (IL)-3 or erythropoietin (EPO) receptor, activate the MAP kinase/ERK (extracellular signal-regulated kinases) cascade. MAP kinases play an important role in hematopoiesis. Most hematopoietic cytokines activate the JAK-STAT and Ras-ERK pathways, both of which are required for sufficient proliferation and differentiation of hematopoietic cells. MAP kinases also play a critical role in megakaryopoiesis induced by c-mpl. However, little is known regarding the regulation of MAP kinase in hematopoietic cells. Recently, we cloned a family of novel membrane bound molecules, Spreds, which are c-kit binding proteins related to Sprouty. Drosophila Sprouty was identified as a negative regulator of ERK activation induced by several growth factors, including ***FGF*** and EGF. Four Sprouty homologues have been identified in mammals. Vertebrate Sproutys have been implicated in negative-feedback regulation of ***FGF***-signaling in embryogenesis and ***angiogenesis***, although their mechanism of inhibition remains controversial. We have identified three Spred family proteins in mammals, which have a Sprouty-related C-terminal cysteine rich (SPR) domain, in addition to an N-terminal Ena/VASP homology (EVH) 1 domain. The SPR-domain of Sprouty, and probably Spred, is palmitoylated, causing localization to the membrane fraction. Like Sprouty, Spred-1, Spred-2, and Spred-3 also downregulate Ras/ERK signaling. We have shown that Spred interacts with ras and inhibits Raf kinase activation without reducing Ras activation, and interestingly, it also stabilizes EGF-induced Raf-1 translocation from the cytosol to the plasma membrane. As Spred inhibits Ras-induced ERK activation, it might modulate unidentified steps

of Raf activation by a novel mechanism. Moreover, a C-terminal deletion mutant of Spred-1 functions as a dominant negative and augments serum and NGF-induced ERK activation. The physiological function of Spred/Sprouty family proteins remains to be investigated. Spred-1 expression was reported to be high in the brain and ***heart***, and we found that it is also highly expressed in hematopoietic cells. To investigate the role of Spred-1 in hematopoietic cells, we expressed Spred-1 in IL-3- and SCF-dependent cell lines as well as hematopoietic progenitor cells from mouse ***bone***-marrow*** using retroviral gene transfer. In IL-3 dependent Ba/F3 cells expressing c-kit, forced expression of Spred-1 reduced the proliferation rate and decreased ERK activation in response to IL-3 and SCF. SCF-dependent cell migration was also suppressed by wild-type Spred-1 overexpression. In contrast, a dominant negative form of Spred-1, dC-Spred, augmented proliferation and cell migration. Furthermore, wild-type Spred-1 strongly inhibited colony formation in ***bone***-marrow*** cells from mice, whereas dC-Spred enhanced colony formation. These data suggest that Spred-1 acts as a negative regulator of hematopoiesis by regulating hematopoietic growth factor-induced MAP kinase activation in mice. The finding of a negative regulator of cytokine-induced ERK activation facilitates the study of ERK function in hematopoiesis and may be useful for in vitro manipulation of hematopoietic progenitor cell expansion.

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AN 2003:356825 BIOSIS <<LOGINID::20070126>>

DN PREV200300356825

TI Comparison of Umbilical Cord Blood Versus ***Bone***-Marrow***-Derived Endothelial Precursor Cells in Mediating Neovascularization in a NOD/SCID Hind ***Limb*** Injury Model.

AU Finney, M. [Reprint Author]; Martin, J. [Reprint Author]; Swan, J. [Reprint Author]; Kadereit, S. [Reprint Author]; Kozik, M. [Reprint Author]; Emancipator, S. [Reprint Author]; Pomplii, V. [Reprint Author]; Haynesworth, S. [Reprint Author]; Fu, P. [Reprint Author]; Laughlin, M. J. [Reprint Author]

CS Medicine, Case Western Reserve University, Cleveland, OH, USA

SO Blood, (***November 16 2002***) Vol. 100, No. 11, pp. Abstract No. 2691. print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Aug 2003

Last Updated on STN: 6 Aug 2003

AB It has been reported that endothelial precursor cells (EPCs) for potential use in therapeutic ***angiogenesis*** can be derived from either umbilical cord blood (UCB) or adult ***bone***-marrow*** (BM). We compared both stem cell sources of EPC in a hind- ***limb*** ischemia*** model in the NOD/SCID mouse. Density gradient centrifugation was used to isolate mononuclear cells (MNC) from fresh UCB or BM. Cells were plated on fibronectin coated tissue culture flasks at a density of 4-6 x 10⁶ cells/ml (UCB MNC) or 1-2 x 10⁶ cells/ml (BM MNC) in EBM2 medium (Clonetics) with 5% FBS and standard SingleQuot additives that included VEGF, ***FGF***, IGF, hydrocortisone, ascorbic acid, heparin (Kalka et al. (2000) PNAS 97:3422-3427). Non-adherent cells were removed after 4 days of culture and medium was changed every fourth day thereafter. During the second week of culture, cells adopted the spindle-like morphology characteristic for EPCs. At Day 6-7 cells were trypsinized and counted. Adherent cell yield from UCB cultures were on average 2.5% of initial MNC input, compared to 21.5% obtained from BM MNC. Endothelial characteristics were verified in both cultures by uptake of DiI-labeled acetylated low density lipoprotein and adherence of FITC-conjugated Ulex Europarus lectin visualized by fluorescent microscopy and positive CD31 staining characterized by flow cytometry. Next, 1 x 10⁶ cells were injected into hind- ***limb*** injured mice. For this, a sub-lethal dose of irradiation was given to athymic NOD/SCID mice, and the right femoral artery of each mouse was isolated, ligated and transected at the inguinal ligament level. Immediately after surgery and injection of cells, baseline blood flow of both the ischemic right leg and the non-operated left leg was measured using a laser Doppler flowmeter. Study mice were injected with EPC cells derived from either UCB or BM. Control mice were injected with saline or complete EBM2 medium. Laser Doppler measurements of both hind limbs were taken on days 7, 14 and 28 and tissue samples from lower calf muscle were harvested at day 28 for histological studies. A ratio of perfusion in the ischemic/healthy ***limb*** was used to compare neovascularization in the three study groups. Immediately following femoral ligation the perfusion ratios were 0.057 +/- 0.011 (control group), 0.029 +/- 0.007 (UCB-derived EPC) and 0.018 +/- 0.012 (BM-derived EPC) showing reduced perfusion in all groups. After 14 days, there was a statistically significant difference between groups receiving EPCs compared to the control group. Perfusion ratios in the control group remained low, with 0.24 +/- 0.032 (n=14) compared to 0.41 +/- 0.031 (n=22) in the mouse group receiving UCB-derived EPC (p=0.0008) and 0.42 +/- 0.063 (n=7) in the mouse group receiving BM-derived EPC (p=0.0086). Importantly, there was no significant difference between the two sources of EPCs (p=0.8317). However, after 28 days perfusion ratios of mice that received BM-derived EPCs dropped below control mice while perfusion ratios of mice that received UCB-derived EPCs remained higher than control mice. This observation did not attain statistical significance. Taken together,

these results point to possible differences in characteristics of EPC derived from UCB vs BM sources.

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AN 2003:356472 BIOSIS <<LOGINID::20070126>>

DN PREV200300356472

TI Role of ENOS and INOS in Hemangioblast Activity and ***Blood*** **Vessel*** **Formation***

AU Guthrie, Steven M. [Reprint Author]; Brown, Gary A. J. [Reprint Author]; Caballero, Sergio [Reprint Author]; Grant, Maria B. [Reprint Author]; Scott, Edward W. [Reprint Author]

CS Program in Stem Cell Biology, University of Florida, Gainesville, FL, USA

SO Blood, (***November 16 2002***) Vol. 100, No. 11, pp. Abstract No. 458, print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA, December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Aug 2003

Last Updated on STN: 18 Sep 2003

AB Endothelial and Inducible Nitric Oxide Synthases (ENOS/INOS) perform in many physiological processes including wound healing, increasing vascular permeability, decreasing blood pressure, and vessel remodeling. Recently our lab has shown that adult hematopoietic stem cell (HSC) can provide functional hemangioblast activity. We hypothesize that ENOS and INOS play an important role in new ***blood*** **vessel*** **formation*** and hemangioblast activity. ENOS and INOS knock-out animals were transplanted with highly purified (c-kit⁺, sca-1⁺) green fluorescent protein (gfp) ***bone*** **marrow***. After multilineage reconstitution was established rAAV-VEGF was administered and one month later retinal ***ischemia*** was induced. The resulting neovascularization was quantitated via serial section staining, immunohistochemistry, and confocal microscopy. The two isoforms of the ***NOS*** enzymes have diametrically opposite effects on the type and amount of neovascularization. The INOS deficiency yielded vessels which were gfp positive indicating that the transplanted HSC contributed to the vessel formation. These vessels were highly branched and were shown to be functional when the circulatory system was perfused with a fluorescent dye. In contrast, ENOS deficiency produced only very large non-branched gfp blood vessels, which could not be perfused. The untreated eye of the ENOS knockout animal also exhibited the same architecture indicating that additional injury is not necessary due to the constant turnover of vessels in these animals. These results suggest that alteration in ***NOS*** activity or NO levels can be used to control the size and branching of new vessels formed by the hemangioblast. We are currently testing the effects of pharmacologic agents affecting ***NOS*** /NO on hemangioblast activity.

L17 ANSWER 11 OF 27 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2003:79552 BIOSIS <<LOGINID::20070126>>

DN PREV200300079552

TI Stimulation of nicotinic acetylcholine receptors promotes proliferation, activation and homing of endothelial progenitor cells during ***ischemia***

AU Heesch, Christopher [Reprint Author]; Johnson, Frances L.;

Pathak-Gulati, Anjali; Cooke, John P.

CS Frankfurt Univ, Frankfurt, Germany

SO Circulation, (***November 5 2002***) Vol. 106, No. 19 Supplement, pp. II-64, print.

Meeting Info.: Abstracts from Scientific Sessions. Chicago, IL, USA.

November 17-20, 2002. American Heart Association.

ISSN: 0009-7322 (ISSN print).

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Feb 2003

Last Updated on STN: 6 Feb 2003

L17 ANSWER 12 OF 27 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2001:264108 BIOSIS <<LOGINID::20070126>>

DN PREV200100264108

TI The effect of transendocardial delivery of autologous ***bone*** **marrow*** stimulated by Granulocyte Monocyte Colony Stimulating Factor (***GM*** - ***CSF***) on ischemic ***myocardial*** perfusion and function.

AU Fuchs, Shmuel [Reprint author]; Baffour, Richard [Reprint author]; Shou, Matie [Reprint author]; Zhou, Yi Fu [Reprint author]; Tio, Fermin O.

[Reprint author]; Leon, Martin B. [Reprint author]; Epstein, Stephen E.

[Reprint author]; Kornowski, Ran [Reprint author]

CS Cardiovascular Research Institute, Washington Hospital Center, Washington, DC, USA

SO Journal of the American College of Cardiology, (***February, 2001***) Vol. 37, No. 2 Supplement A, pp. 246A, print.

Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology. Orlando, Florida, USA. March 18-21, 2001. American College of Cardiology.

CODEN: JACCDI. ISSN: 0735-1097.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 30 May 2001

Last Updated on STN: 19 Feb 2002

L17 ANSWER 13 OF 27 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2000:530295 BIOSIS <<LOGINID::20070126>>

DN PREV200000530295

TI Transendocardial delivery of autologous ***bone*** **marrow*** enhances collateral perfusion and regional function in pigs with chronic experimental ***myocardial*** **ischemia***

AU Kornowski, R. [Reprint author]; Fuchs, S. [Reprint author]; Baffour, R. [Reprint author]; Shou, M. [Reprint author]; Leon, M. B.; Epstein, S. E. [Reprint author]

CS Cardiovascular Research Institute, Washington Hospital Center, Washington, DC, USA

SO European Heart Journal, (***August-September, 2000***) Vol. 21, No. Abstract Supplement, pp. 356, print.

Meeting Info.: XXII Congress of the European Society of Cardiology.

Amsterdam, Netherlands. August 26-30, 2000. European Society of Cardiology.

CODEN: EHJODF. ISSN: 0195-668X.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 6 Dec 2000

Last Updated on STN: 11 Jan 2002

L17 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:235074 CAPLUS <<LOGINID::20070126>>

DN 144:280643

TI Conditioned medium of autologous or allogenic ***bone***

marrow progenitor cells for ***angiogenesis*** treatment

IN Kornowski, Ran; Fuchs, Shmuel; Epstein, Stephen E.; Leon, Martin B.

PA Myocardial Therapeutics, Inc., USA

SO U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 618,183.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006057722	A1	20060316	US 2005-221469	20050907
WO 2000057922	A1	20001005	WO 2000-US8353	20000330 <-
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 7097832	B1	20060829	US 2001-868411	20010614
US 2004131601	A1	20040708	US 2003-618183	20030710
WO 2006029262	A2	20060316	WO 2005-US31982	20050907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 1999-126800P P 19990330

US 1999-138379P P 19990609

WO 2000-US8353 W 20000330

US 2001-868411 A2 20010614

US 2002-160514 B2 20020530

US 2003-618183 A2 20030710

US 2004-608272P P 20040908

AB A therapeutic compn. is provided that comprises a cell-free conditioned medium contg. mixed secretion products of isolated ***angiogenic*** progenitor cells obtained from ***bone*** **marrow***, peripheral blood, or adipose tissue. The compn. may addnl. contain ***angiogenesis*** -promoting proteins obtained by transfecting the progenitors cells in culture with an ***angiogenesis*** promoting transgene. The compn. is useful to promote ***angiogenesis*** when introduced into or adjacent to an ischemic site in a patient, such as in ***myocardium*** or peripheral ***limb***. Methods are also provided for utilizing such cell-free conditioned medium to deliver ***angiogenesis*** -promoting proteins to a patient. The cell-free conditioned medium can also be injected into the blood stream for delivery

to the ischemic tissue. The cells can derive from either an autologous or allogenic source and can be lyophilized or frozen for storage.

L17 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2004:80349 CAPLUS <<LOGINID::20070126>>
DN 140:146136

TI Preparation of chemokine receptor binding (benzimidazol-2-ylmethyl)(5,6,7,8-tetrahydroquinolin-8-yl)amines and related heterocyclic compounds with enhanced efficacy against AIDS and other disorders
IN Bridger, Gary; Kaller, Al; Harwig, Curtis; Skerlj, Renato; Bogucki, David; Wilson, Trevor R.; Crawford, Jason; McEachern, Ernest J.; Atsma, Bern; Nan, Siqiao; Zhou, Yuanxi; Schols, Dominique; Smith, Christopher D.; Di Fluri, Maria R.

PA USA

SO U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 446,170.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004019058	A1	20040129	US 2003-457034	20030606
US 2003220341	A1	20031127	US 2002-329329	20021223 <--
CA 2522535	A1	20041209	CA 2004-2522535	20040521
WO 2004106493	A2	20041209	WO 2004-US15977	20040521
WO 2004106493	A3	20050825		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1628533	A2	20060301	EP 2004-752905	20040521
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
ZA 2004004589	A	20050909	ZA 2004-4589	20040609
US 2006100240	A1	20060511	US 2005-301725	20051213
PRAI US 2001-342716P	P	20011221		
US 2002-350822P	P	20020117		
US 2002-329329	A2	20021223		
US 2003-446170	A2	20030523		
US 2003-457034	A	20030606		
WO 2004-US15977	W	20040521		

OS MARPAT 140:146136
GI

/ Structure 1 in file .gra /

AB The invention relates to heterocyclic compds. (shown as I; e.g. (1H-benzimidazol-2-ylmethyl)(piperidin-3-ylmethyl)(5,6,7,8-tetrahydroquinolin-8-yl)amine trihydrobromide) consisting of a core N atom surrounded by three pendant groups, wherein two of the three pendant groups are preferably benzimidazolylmethyl and tetrahydroquinolyl, and the 3rd pendant group contains N and optionally contains addnl. rings. The compds. bind to chemokine receptors, including CXCR4 and CCR5, and demonstrate protective effects against infection of target cells by a human immunodeficiency virus (HIV). Many I exhibit IC50 values of 5-5.5 nM for inhibition of HIV-1 (NL4.3) replication in peripheral blood mononuclear cells and 5 nM-5 .mu.M for inhibition of SDF-1.alpha. induced Ca flux in CCRF-CEM cells, a T-lymphoblastoid cell line that expresses CXCR4. It is also stated that the compds. I behave in a manner similar to 1,1'-(1,4-phenylene-bis(methylene))-bis-1,4,8,11-tetraazacyclotetradecane (AMD3100) which showed to elevate progenitor cell levels (data given). Although the methods of prepn. are not claimed, >170 example preps. are included. For I: X and Y = N or CR1; Z is S, O, NR1 or CR12; each R1-R6 = H or a noninterfering substituent; n1 is 0-4; n2 is 0-1, wherein the a signifies C.tpbond.C may be substituted for CR5:CR5; n3 is 0-4; wherein n1 + n2 + n3 = .gtoreq. 2; b is 0-2; wherein the following combinations of R groups may be coupled to generate a ring, which ring may be (un)satd.: R2 + R2, one R2 + R3, R3 + one R4, R4 + R4, one R5 + another R5, one R5 + one R6, and R6 + R6; wherein the ring may not be arom. when the participants in ring formation are two R5; and wherein when n2 is 1, neither n1 nor n3 can be 0.

L17 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2003:971808 CAPLUS <<LOGINID::20070126>>
DN 140:13049

TI Intramyocardial injection of autologous ***bone*** ***marrow***
IN Epstein, Stephen; Fuchs, Shmuel; Kornowski, Ran; Leon, Martine B.; Carpenter, Kenneth W.

PA Myocardial Therapeutics, Inc., USA

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2003101201	A1	20031211	WO 2003-US15529	20030516 <--
W: AU, CA, JP				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				

CA 2487410	A1	20031211	CA 2003-2487410	20030516 <--
AU 2003232152	A1	20031219	AU 2003-232152	20030516 <--
EP 1513404	A1	20050316	EP 2003-756182	20030516

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP 2005527228	T	20050915	JP 2004-508572	20030516

PRAI US 2002-160514 A 20020530

WO 2003-US15529 W 20030516

AB Methods are provided for enhancing transfection efficiency of ***bone*** ***marrow*** cells by transfecting early attaching cells derived from ***bone*** ***marrow*** in culture. Methods are also provided for utilizing such early attaching cells derived from autologous ***bone*** ***marrow*** to deliver ***angiogenesis*** -promoting transgenes to a patient. The transfected early attaching cells are introduced into an ischemic tissue, such as the ***heart***, to enhance formation of collateral blood vessels. Methods are also provided for treating ischemic muscle by co-administration of autologous ***bone*** ***marrow*** cells and RGTA, for example RGTA11.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:596061 CAPLUS <<LOGINID::20070126>>

DN 139:346004

TI Therapeutic ***angiogenesis*** for ischemic ***heart*** disease by transplantation of ***bone*** ***marrow*** stem cells

AU Iba, Osamu; Matsubara, Hiroaki; Iwasaka, Toshiji

CS Dep. of Cardiovascular Center and Medicine II, Kansai Medical University, Japan

SO Jikken Igaku (***2003***), 21(8), 1122-1128

CODEN: JIIGEF; ISSN: 0288-5514

PB Yodoshia

DT Journal; General Review

LA Japanese

AB A review, on roles of ***angiogenic*** factors (VEGF), ***angiogenic*** factor genes, and ***angiogenic*** cytokines (***GM*** - ***CSF***, G-CSF) in the therapeutic ***angiogenesis*** for ischemic ***heart*** disease by transplantation of ***bone*** ***marrow*** stem cells.

L17 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:405683 CAPLUS <<LOGINID::20070126>>

DN 140:125908

TI The clinical impact of vascular growth factors and endothelial progenitor cells in the acute coronary syndrome

AU Wang, Yongzhong; Johnsen, Hans E.; Jorgensen, Erik; Kastrup, Jens

CS Med. Dep. B, Cardiac Catheterization Lab., Univ. Hosp., Copenhagen, Den.

SO Scandinavian Cardiovascular Journal (***2003***), 37(1), 18-22

CODEN: SCJOFY; ISSN: 1401-7431

PB Taylor & Francis Ltd.

DT Journal; General Review

LA English

AB A review on the two vascular growth factors (VEGF) and ***FGF*** and on ***bone*** - ***marrow*** -derived endothelial progenitor cells (EPCs) in the development of new blood vessels in patients with the acute coronary syndrome. It focuses on the natural acute and early changes of these ***angiogenic*** factors, to reach a consensus, which might become a basis for new ideas on treatment regimes in the acute coronary syndrome.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:154455 CAPLUS <<LOGINID::20070126>>

DN 138:199989

TI Novel human .alpha.CP isoforms, binding of .alpha.CP and HuR, and uses thereof for modulating gene expression, stabilizing hypoxia regulated mRNAs (such as VEGF) and inducing ***angiogenesis***

IN Guy, Louis-Georges

PA Angiogene Inc., Can.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

PI WO 2003016343	A2	20030227	WO 2002-CA1275	20020816 <--
WO 2003016343	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002322911 A1 20030303 AU 2002-322911 20020816 <--
US 2004241797 A1 20041202 US 2004-486865 20040213
PRAI US 2001-312397P P 20010816
WO 2002-CA1275 W 20020816

AB The present inventor has discovered novel human .alpha.CP isoforms, .alpha.CP1A, .alpha.CP1B, .alpha.CP2A, and .alpha.CP2B. The present inventor has also discovered that .alpha.CP polypeptides and HuR bind each other. The present inventor has further discovered that .alpha.CP polypeptides are capable of binding mRNAs mols., such as VEGF mRNA, for stabilizing the same. The present inventor has further discovered that HuR is capable of binding mRNA mols. previously unknown to be bound by HuR. The invention also describes mRNA stabilizing elements and consensus sequences involved in binding of .alpha.CP1, .alpha.CP2 and HuR proteins to mRNAs. In general, the invention features an isolated or purified nucleic acid mol. that encodes or corresponds to a human .alpha.CP. The present invention describes methods for modulating gene expression, stabilizing VEGF mRNAs, for inducing ***angiogenesis***, for treating various mammalian diseases including coronary and cardiac diseases and for identifying modulators of gene expression by using human proteins called .alpha.CP1, .alpha.CP2 and HuR.

L17 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2002:906282 CAPLUS <<LOGINID::20070126>>

DN 138:8310

TI Hypoxia-inducing factors for inducing ***angiogenesis*** and improving muscular functions

IN Guy, Louis-Georges

PA Angiogene Inc., Can.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002094862	A2	20021128	WO 2002-CA752	20020523 <--
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WO 2002094862	A3	20030220		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2447958 A1 20021128 CA 2002-2447958 20020523 <--

US 2003026793 A1 20030206 US 2002-154386 20020523 <--

EP 1395609 A2 20040310 EP 2002-729712 20020523

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2005505252 T 20050224 JP 2002-592336 20020523

PRAI US 2001-292630P P 20010523

US 2002-354529P P 20020208

WO 2002-CA752 W 20020523

AB This invention provides ***HIF*** -3.alpha. nucleic acid and sequences. Also provided are methods for using ***HIF*** -3.alpha. nucleic acids, proteins, fragments, antibodies, probes, and cells, to characterize ***HIF*** -3.alpha., modulate ***HIF*** -3.alpha. cellular levels, induce ***angiogenesis***, improve muscular functions, and treat coronary and cardiac diseases in mammals.

L17 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2002:827183 CAPLUS <<LOGINID::20070126>>

TI Improvement of Collateral Perfusion and Regional Function by Implantation of Peripheral Blood Mononuclear Cells Into Ischemic Hibernating ***Myocardium***

AU Kamihata, Hiroshi; Matsubara, Hiroaki; Nishiue, Takashi; Fujiyama, Soichiro; Amano, Katsuya; Iba, Osamu; Imada, Takanobu; Iwasaka, Toshiiji
CS Department of Medicine II and Cardiovascular Center, Kansai Medical University, Moriguchi, Osaka, Japan

SO Arteriosclerosis, Thrombosis, and Vascular Biology (***2002***),

22(11), 1804-1810

CODEN: ATVBFA; ISSN: 1079-5642

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Objective-This study was performed to evaluate the ***angiogenic*** effect of implantation of peripheral blood mononuclear cells (PB-MNCs) compared with ***bone*** ***marrow*** mononuclear cells (BM-MNCs) into ischemic hibernating ***myocardium***. Methods and Results-A NOGA electromech. system was used to map the hibernating region and to inject cells. PB-MNCs and BM-MNCs contained similar levels of vascular endothelial growth factor and basic fibroblast growth. ***Nos*** . of endothelial progenitors were approx. 500-fold higher in BM-MNCs. In BM-MNC-implanted ***myocardia*** of pigs, an increase in systolic function (ejection fraction from 33% to 52%) and regional blood flow (.1-fold) and a redn. of the ischemic area (from 29% to 8%) were obsd. PB-MNC implantation reduced the ischemic area (from 31% to 17%), the

extent of which was less than that seen with BM-MNCs. In saline-implanted ***myocardium***, the ischemic area expanded (from 28% to 38%), and systolic function deteriorated. Angiog. revealed an increase in collateral vessel formation by PB-MNC or MB-MNC implantation. Capillary ***nos*** . were increased 2.6- and 1.7-fold by BM-MNC and PB-MNC implantation, resp. BM-MNCs but not PB-MNCs were incorporated into neocapillaries. Conclusions-Catheter-based implantation of PB-MNCs can effectively improve collateral perfusion and regional function in hibernating ischemic ***myocardium*** by its ability to mainly supply ***angiogenic*** factors and cytokines.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2002:637539 CAPLUS <<LOGINID::20070126>>

DN 137:163807

TI Localized ***myocardial*** injection method for treating ischemic ***myocardium***

IN Palasis, Maria

PA Boston Scientific Corporation, USA

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002064157	A2	20020822	WO 2002-US3118	20020123 <--
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WO 2002064157	A9	20030605		
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WO 2002064157	A3	20030807		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2433936 A1 20020822 CA 2002-2433936 20020123 <--

US 2002172663 A1 20021121 US 2002-57409 20020123 <--

EP 1361896 A2 20031119 EP 2002-720895 20020123 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2005501802 T 20050120 JP 2002-563950 20020123

PRAI US 2001-263468P P 20010123

WO 2002-US3118 W 20020123

AB This invention relates to a method of treating ischemic or diseased ***myocardium*** by injecting a therapeutic agent, such as a gene, protein, cell or drug, into normal ***myocardium***, preferably adjacent to an ischemic zone in the ***heart*** of a subject. The method is useful for inducing ***angiogenesis*** and collateral ***blood*** ***vessel*** ***formation*** to improve cardiac function in subjects with ischemic ***heart*** disease. The method can also be used to promote tissue regeneration in such subjects.

L17 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2002:185320 CAPLUS <<LOGINID::20070126>>

DN 136:242932

TI Identification of peptide ligands for specific cell types by phage display for use in drug targeting and control of biological processes

IN Arap, Wadhi; Pasqualini, Renata

PA Board of Regents, the University of Texas System, USA

SO PCT Int. Appl., 311 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002020769	A1	20020314	WO 2001-US27692	20010907 <--
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WO 2002020769	A9	20030904		
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2421271 A1 20020314 CA 2001-2421271 20010907 <--

AU 2001088843 A5 20020322 AU 2001-88843 20010907 <--

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004508045 T 20040318 JP 2002-525776 20010907

CA 2458047 A1 20030320 CA 2002-2458047 20020830 <--

WO 2003022991 A2 20030320 WO 2002-US27836 20020830 <--

WO 2003022991 A3 20041028

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

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EP 1497314 A2 20050119 EP 2002-757531 20020830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

CA 2496938 A1 20040311 CA 2002-2496938 20021030
WO 2004020999 A1 20040311 WO 2002-US34987 20021030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002364501 A1 20040319 AU 2002-364501 20021030
EP 1546714 A1 20050629 EP 2002-799873 20021030

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2004170955 A1 20040902 US 2003-363204 20031006
US 2005003466 A1 20050106 US 2004-784537 20040223
US 2006094672 A1 20060504 US 2004-489071 20041013
US 2006239968 A1 20061026 US 2006-530168 20060223

PRAI US 2000-231266P P 20000908
US 2001-765101 A 20010117
WO 2001-US27692 W 20010907
WO 2002-US27836 W 20020830
WO 2002-US34987 W 20021030

AB The present invention concerns methods and compns. for in vivo and in vitro targeting. A large no. of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting ***angiogenesis***, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing wt. loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:904279 CAPLUS <<LOGINID::20070126>>
DN 136:32173

TI Identification and use of human ***bone*** ***marrow*** -derived endothelial progenitor cells to improve ***myocardial*** function after ischemic injury

IN Iltescu, Silviu
PA The Trustees of Columbia University In the City of New York, USA
SO PCT Int. Appl., 157 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001094420	A1	20011213	WO 2001-US18399	20010605 <-
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412436	A1	20011213	CA 2001-2412436	20010605 <-
EP 1290033	A1	20030312	EP 2001-942041	20010605 <-
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509847	T	20040402	JP 2002-501968	20010605
US 2004131585	A1	20040708	US 2003-220554	20030304
US 2006111290	A1	20060525	US 2005-234879	20050922
PRAI US 2000-587441	A2	20000605		
WO 2001-US18399	W	20010605		
US 2003-220554	A1	20030304		

AB The present invention provides a method of stimulating vasculogenesis of ***myocardial*** infarct damaged tissue in a subject comprising: (a) removing stem cells from a location in the subject; (b) recovering endothelial progenitor cells in the stem cells; (c) introducing the

endothelial progenitor cells from step (b) into a different location in the subject such that the precursors migrate to and stimulate revascularization of the tissue. The stem cells may be removed directly or by mobilization. The endothelial progenitor cells may be expanded before introduction into the subject. The present invention further provides a method of inducing ***angiogenesis*** in perinfarct tissue. The present invention further provides a method of selectively increasing the trafficking of human ***bone*** ***marrow*** -derived endothelial cell precursors to the site of tissue damaged by ischemic injury which comprises: (a) administering endothelial progenitor cells to a subject; (b) administering chemokines to the subject so as to thereby attract endothelial cell precursors to the ischemic tissue. The present invention provides a method of stimulating vasculogenesis or ***angiogenesis*** of ***myocardial*** infarct damaged tissue in a subject comprising injecting allogeneic stem cells into a subject. The present invention further provides a method of improving ***myocardial*** function in a subject that has suffered a ***myocardial*** infarct comprising any of the instant methods. The present invention further provides a method of improving ***myocardial*** function in a subject that has suffered a ***myocardial*** infarct comprising injecting G-CSF or anti-CXCR4 antibody into the subject in order to mobilize endothelial progenitor cells.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:707023 CAPLUS <<LOGINID::20070126>>
DN 133:261527

TI Intramyocardial injection of autologous ***bone*** ***marrow*** for treatment of cardiac or ***myocardial*** conditions

IN Kornowski, Ran; Fuchs, Shmuel; Epstein, Stephen E.; Leon, Martin B.
PA USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000057922	A1	20001005	WO 2000-US8353	20000330 <-
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368677	A1	20001005	CA 2000-2368677	20000330 <-
EP 1171165	A1	20020116	EP 2000-919831	20000330 <-
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002540176	T	20021126	JP 2000-607671	20000330 <-
AU 767402	B2	20031106	AU 2000-40452	20000330 <-
US 7097832	B1	20060829	US 2001-868411	20010614
US 2004131601	A1	20040708	US 2003-618183	20030710
US 2004161421	A1	20040819	US 2004-776545	20040210
US 2006051334	A1	20060309	US 2005-117607	20050427
US 2006057722	A1	20060316	US 2005-221469	20050907
PRAI US 1999-126800P	P	19990330		
US 1999-138379P	P	19990609		
WO 2000-US8353	W	20000330		
US 2001-868411	A2	20010614		
US 2002-160514	A2	20020530		
US 2003-618183	A2	20030710		
US 2004-566332P	P	20040428		
US 2004-608272P	P	20040908		

AB A method of treating cardiac or ***myocardial*** conditions comprises the administration of an effective amt. of autologous ***bone*** ***marrow***. The ***bone*** ***marrow*** may optionally be stimulated and/or administered in combination with a pharmaceutical drug, protein, gene, or other factor or therapy that may enhance ***bone*** ***marrow*** prodn. of ***angiogenic*** growth factors and/or promote endothelial cell proliferation or migration or ***blood*** ***vessel*** ***formation***.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:487368 CAPLUS <<LOGINID::20070126>>
DN 131:99540

TI Purified populations of stem cells

IN Rafii, Shahin; Witte, Larry; Moore, Malcolm A. S.
PA Imclone Systems Incorporated, USA; Cornell Research Foundation, Inc.; Sloan-Kettering Institute for Cancer Research
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9937751	A1	19990729	WO 1999-US1517	19990125 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002051762	A1	20020502	US 1998-12903	19980123 <--
CA 2311729	A1	19990729	CA 1999-2311729	19990125 <--
AU 9924692	A	19990809	AU 1999-24692	19990125 <--
EP 1060242	A1	20001220	EP 1999-904250	19990125 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002500879	T	20020115	JP 2000-528659	19990125 <--
PRAI US 1998-12903	A2	19980123		
US 1998-72362P	A2	19980123		
WO 1999-US1517	W	19990125		
AB The invention is directed to a purified population of mammalian endothelial, muscle, or neural stem cells. The invention further provides methods for isolating such populations of cells; methods for using such populations of cells for treating mammals; methods for making vectors for gene therapy; and methods for carrying out gene therapy with such vectors.				
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD				
ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L17 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:550492 CAPLUS <<LOGINID::20070126>>
DN 129:170526
TI Methods for modulating hematopoiesis and vascular growth
IN Baron, Margaret H.; Farrington, Sarah M.; Belaussoff, Maria
PA The President and Fellows of Harvard College, USA
SO PCT Int. Appl., 77 pp.
CODEN: P1XXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9835020	A2	19980813	WO 1998-US2633	19980210 <--
WO 9835020	A3	19990114		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2280736	A1	19980813	CA 1998-2280736	19980210 <--
EP 1019490	A2	20000719	EP 1998-906314	19980210 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001511650	T	20010814	JP 1998-535042	19980210 <--
US 2001041668	A1	20011115	US 1998-21660	19980210 <--
US 6713065	B2	20040330		
US 2005002933	A1	20050106	US 2004-772090	20040203
PRAI US 1997-37513P	P	19970210		
US 1997-49763P	P	19970616		
US 1998-21660	A1	19980210		
WO 1998-US2633	W	19980210		

AB Methods and assays are provided for selecting compds. that are functionally equiv. to a gene product expressed in an embryo's extraembryonic tissue for use in modulating hematopoiesis and vascular growth, such compd. being exemplified by a hedgehog protein, and an agonist of a hedgehog protein binding receptor. According to the method, such compd. causes undifferentiated mesodermally derived cells to undergo at least one of hematopoiesis or vasculogenesis. Examples of undifferentiated mesodermally derived cells include hematopoietic stem cells and embryonic explant cells. The method of the invention may be used to treat a variety of pathol. conditions, including developmental errors in vascular growth or hematopoiesis and pathol. conditions arising from abnormal ***nos*** of erythroid cells, or abnormally enhanced vascular growth.

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LAST RELOADED: Jan 19, 2007 (20070119/UP).

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